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THE
LISTER MEMORIAL LECTURE

Delivered in the Theatre

of the

Royal College of Surgeons of England

on April 5, 1933

by

SIR CHARLES BALLANCE

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To

the Memory of

A. C. B.

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Mr President,

We are gathered together this afternoon to celebrate an act of remembrance to the noble character and immortal achievements of Joseph Lister. I am very proud to stand here as a witness on this Lister anniversary.

The whole life of Joseph Lister, all his physical strength, all the high attainments of his mind, were consecrated to the sacred surgical mission of winning control over septic diseases which are so fatal to the life of man. Lister had no other ambition but to serve. He desired no other recompense than the feeling of duty accomplished. This continual devotion to a noble purpose proved in him the source of an ever-widening river of happiness.

He might have said :—

" Yes, let them go, gain fashion, pleasure, power,
And all the busy elves to whose domain
Belongs the nether sphere, the fleeting hour.

* * * * *

" Mine is the world of thought. . . . Mine,
The sense of beauty and the thirst for truth." [1]

Lister is the upper light of our art and science, for before his time the pathway of surgery was shrouded in " darkness, clouds, and thick darkness." [2] He has bequeathed to us an imperishable record and a precious example.

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1. Lines written by Macaulay in 1847. 2. Deut. Chap. 4, v. 11.

Whether I am visiting a surgical operating theatre in a lonely isle of the Pacific, or one in some great city, I sense in it the living spirit of Lister. His labours have ransomed countless numbers of our race from pain, from illness and from death; and the lapse of time is powerless to dim their lustre. History has deliberately pronounced that, among eminent men, no one has left a more stainless and none a more splendid name. "The whole earth is the sepulchre of Lister. In this land and on far off shores there is an abiding memorial; that best of all memorials, 'begot in the ventricle of memory.'[3] No pen or chisel has traced it; it is graven, not on marble or brass, but in the hearts of men."[4]

The Early Professional Life of Lister.

During the period of Lister's early professional life he came under the influence of men famous in physiology, in chemistry, in physics and in the use of the microscope. All action has its origin in thought, and Lister developed an outstanding aptitude for mental concentration upon the definite problem to be solved. He was gifted with the habit of untiring industry, with luminous mental insight, and with a high ideal of life. These were combined with an unusual acquaintance with the sciences of physiology and chemistry. It was natural, therefore, that his early studies were directed to the fundamental problems of physiology and pathology. His first contributions to scientific literature formed a grand foundation on which to build those discoveries which have so transformed and enriched surgical knowledge and practice.

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3. "Love's Labour Lost." Act IV. Sc. II.

4. Adapted from a paragraph in a funeral oration by Pericles. Thucydides II. 43.

The titles of some of Lister's early papers are :—

1. The contractile tissue of the iris.[5]
2. The structure of a nerve fibre.[6]
3. The coagulation of the blood.[7]
4. The early stages of inflammation.[8]
5. The nervous mechanism which regulates the contractions of the arteries and the movements of the intestine.[9]
6. The absorption of ligatures by the living tissues. [10]

The experimental labours of Louis Pasteur struck the final blow in 1864 at the doctrine of spontaneous generation. When Lister's attention was called to the conclusions at which Pasteur had arrived, he recognised at once that a flood of light had been thrown on the whole subject of putrefaction in wounds. It was not till the 12th of August, 1865, that Lister was able to put the matter to the test in the case of a compound fracture.[11] The result amply justified his hypothesis that putrefaction in wounds was due to micro-organisms.

Lister contributed many papers dealing with the germ theory of putrefactive changes, but it was not till August 12, 1880, that he gave an address entitled, "On the Relations of Micro-Organisms to Disease." [12]

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5. Quarterly Journal of Microscopical Science. Vol. I, 1853.
6. Quarterly Journal of Microscopical Science. October, 1859.
7. "The causes of coagulation of the blood in diseases of the blood-vessels." Edinburgh Medical Journal, 1858. And "Further researches on the coagulation of the blood." Ibid. Dec., 1859, etc., and Croonian Lecture, Royal Society, 1863.
8. Phil: Trans. 1858.
9. Phil: Trans. 1858, and Proc. of Royal Society, 1858.
10. The antiseptic principles in the practice of Surgery—Brit. Med. Journal, 1867, in which paper is described the ligation of the common carotid of the horse.

    The ligation of arteries on the antiseptic system—Lancet, 1869, in which paper is described the ligation of the carotid of the calf.
11. Lancet, 1867.
12. Quarterly Journal of Microscopical Science, April, 1881.

Lister—London, 1877-1893.

Joseph Lister settled in London in 1877, and was Professor of Clinical Surgery at King's College Hospital from 1877 to 1893. Though only a student, I visited King's College Hospital whenever possible. I had read papers by Lister and Pasteur, and was thrilled with a glimpse of the dawning of a new era in surgery. I witnessed the performance by Lister of the first operation performed in London for transverse fracture of the patella. At a later date I was present at the meeting of the Medical Society of London when Lister described the operation and showed patients on whom the operation had been done.[13] One of the senior surgeons present exclaimed: "C'est magnifique, mais ce n'est pas la chirurgie!" It should be remembered that the elder surgeons held that a wound of the knee joint was an injury likely to be fatal. Lister's first operation for transverse fracture of the patella was performed on October 26, 1877; but his pupil, Hector Cameron, of Glasgow, had performed the operation on March 5, 1877.

During the years following my return from Germany in 1885 I was in various ways brought into contact with Lister. The contact which I most highly prized was an occasional invitation to visit him in his study in Park Crescent. He received me with delightful old-world courtesy and a wise, rare smile of welcome, and then said in his simple way: "Tell me what you have been doing. Have you any microscopical slides to show me?" Lister knew I was interested in certain investigations. About them he would talk to me for an hour or more. Now and then he would ask a question. On leaving Park Crescent, I, a struggling young surgeon, was possessed of the wonderful

13. Brit. Med. Journal, 1883, Vol. II, p. 855 and Med. Soc. Trans. 1884, p. 8.

impression that the great Master had been endeavouring to learn something from what I had done! This was a great encouragement to persevere, and with the friendship of Sir James Paget combined to form the "gold clasp" [14] that locks the secret story of my life.

On first contemplating this lecture my plan was to try and paint in words one of my interviews with Lister. I soon found, however, that a lecture so designed could not be given, as Lister did all the talking. I was a silent listener, endeavouring to memorise all he said.

PERSONAL EXPERIENCES OF THREE RESEARCH LABORATORIES

The National Institute for Research, Hampstead.

During the last twelve years I have been engaged in various investigations chiefly in connection with the anastomosis of nerves. The experiments were for some years carried out at the National Institute for Research. The Medical Research Council granted me every assistance.

At the invitation of Sir Arthur Keith, the microscopical part of the work was done at the Royal College of Surgeons by Mr Stewart and Miss Glasscock. To both of these workers in the College Research Laboratories I am much indebted.

The Laboratories of the Royal College of Surgeons.

When I returned to England one and a half years ago, Sir Arthur Keith asked me to repeat some experiments, involving the cervical sympathetic nerve in the new laboratories of the College. This was done. I have often wandered during the morning round the rooms upstairs, and marvelled

14. "Romeo and Juliet." Act I, Sc. 3.

at the concentrated intellectual solemnity of the scientific worker. At last I reach my eyry, and ponder sadly over the fact that during the last fifty years I had not attained this most excellent scientific standard. But hark! A footstep is heard in the corridor. It is the footstep of the beloved Chief. Now all the rooms resound with laughter and with song. I strain my ears to listen, and softly yet distinctly, I hear the lilting music of

"Scots, wha ha'e wi' Wallace bled." [15]

The Laurelwood Laboratory.

More than three years ago, shortly after my return from Australia, I received a long cable from New York, inviting me to cross the Atlantic and carry out certain experimental investigations. The offer gave me a free hand and promised unlimited opportunities. There were many problems of surgery and of surgical pathology which I desired to make the subject of enquiry. The cable was signed Arthur B. Duel. Despite the fact that I did not know where I was to work, that I had but a slight acquaintance with Arthur B. Duel, and that some of my friends thought I was slightly mad—I sailed for America.

I soon found that Arthur B. Duel was an ideal colleague—that he was a man of amazing energy and enthusiasm, that he was skilled in delicate surgical manipulations and, lastly, that he possessed the gift of real and abiding friendship. He was building a laboratory for research on his own estate at Laurelwood, eighty miles from New York. We promptly studied the plans of the laboratory which we both criticised. Duel said, "Shall we sack the architect? If we keep him we shall have a laboratory such as he thinks we ought to have. If we act as architects, we

15. Burns—"Bannockburn."

shall have the laboratory we want." I protested that I was not an architect: he countered with the statement that he had watched me closely for two or three days, and that he was sure I was a born architect! The architect was sacked and later I was informed that thousands of dollars had been saved. If it had not been for the disastrous financial events in America, Duel and I would still be at work on surgical problems in the Laurelwood Laboratory.

The first lantern slide shows Laurelwood situated on the border of a primeval forest and the laboratory built by Dr Duel. (Figs. 1 and 2).

I will now introduce to you "Old Bill." I ought to know something about him, for we were intimately associated for over six hundred days. He was a fierce Abyssinian holy baboon. He had one defect; perhaps I may call it a moral defect; he hated the sight of a woman. If a woman entered the laboratory Old Bill went into transports of rage, and nothing that I could do would soothe the savage breast. (Fig. 3).

This recalls to me a memory of Marcus Beck, who was a fine surgeon, a remarkable personality, and for whom as a young man I had a kind of rapturous admiration. Perhaps I may have been influenced by the fact that Marcus Beck took interest in some investigations in which I was engaged. While Old Bill hated the sight of a woman Marcus Beck detested the sight of a private patient!

This other baboon, "The Macnab," a Mandril, was an aristocrat. We enjoyed his friendship for over six hundred and twenty days. He was proud of his little tail and of his blue nose. He was shy of being stared at, and was annoyed by crowds. Hence we built him a little house with unbreakable glass windows. It was fixed against the ceiling of the inside cage, which was 20 feet high. In this

little house The Macnab would sit surveying the world from China to Peru: immune from the ribald gaze of the multitude. (Fig. 4).

The baboons were so well fed that after the mid-day meal they yawned all the afternoon, and after drinking 1½ pints of milk at 5.30 p.m. they went to sleep till sunrise the next morning. You can see that Old Bill is yawning. During yawning all the muscles of the face contract, and in this way Dr Duel and I were able to watch for and study the return of voluntary movement in the right side of the face. A fresh nerve graft in each of these baboons was substituted for a portion of the right facial nerve in the aquæduct of Fallopius. (Fig. 5).

I have been interested in the operative treatment of facial palsy for 40 years. I performed the first operation for the relief of this condition in 1895. I wish definitely to state that there is now only one operation for facial palsy, and that is the nerve graft operation in the Fallopian aquæduct. This operation gives far better results than the anastomosis operation, and it brings the operation into harmony with the fundamental principles of surgery which demand that an injury to a nerve (like an injury to an artery) must be treated at the site of injury. Knowing a little of the history of surgery, and of the reaction of the profession to new discoveries and to new operations, I am under no illusion as to the immediate and universal acceptance of the nerve graft operation. I have, however, no shadow of doubt that in 20 years from now the operation will be definitely established in every surgical clinic as the operation of choice for facial palsy.

I spent last May and part of June at Laurelwood completing some experiments with Dr Duel and collecting

DIET OF LARGE BABOONS AT LAURELWOOD.

8 A.M. 1½ PINTS OF MILK MIXED WITH 1 RAW EGG AND 1 TABLESPOONFUL OF CODLIVER OIL.

9 A.M. 2 BANANAS, ½ ORANGE, 3 LUMPS OF SUGAR SOAKED IN CODLIVER OIL.

NOON.		
	MONDAY	CORN ON COB, RICE PUDDING WITH PRUNES, FRESH CABBAGE LEAVES, 1 CUP OF PEANUTS.
	TUESDAY	2 BAKED SWEET POTATOES, 2 RAW CARROTS, HANDFUL OF RAISINS, 1 APPLE, FRESH LETTUCE.
	WEDNESDAY	2 BOILED BEETS, CUP OF PEANUTS, CORN ON COB, 1 APPLE.
	THURSDAY	FRESH CABBAGE LEAVES, 2 BAKED SWEET POTATOES, HANDFUL OF RAISINS.
	FRIDAY	RICE PUDDING WITH PRUNES, 2 RAW CARROTS, CUP OF PEANUTS, 1 APPLE.
	SATURDAY	FRESH LETTUCE, CORN ON COB, CUP OF PEANUTS, 2 BAKED SWEET POTATOES.
	SUNDAY	FRESH CABBAGE LEAVES, HANDFUL OF RAISINS, 1 APPLE, CORN ON COB.

5.30 P.M. EGG AND MILK MIXTURE (1½ PINTS EACH).

specimens. In November I received a letter from my colleague, telling me that since I left he had been able to demonstrate that a degenerated nerve graft—that is a graft taken from a nerve from 8 to 30 days cut off from its central connections—will cause recovery of function in the paralysed muscles in less than half the time that is required when a fresh nerve graft is employed. It appears to me that this discovery is of much surgical importance and is of universal application wherever in the body a nerve graft has to be used. In the coming time surgeons must renounce the use of fresh nerve grafts. The rule is absolute that a degenerated nerve graft must be employed.

Gabriel Fallopius [16] described in 1600 the facial canal in the temporal bone as an aquæduct. He did this, he writes, because it is in the likeness of an aquæduct. No doubt Gabriel was familiar with aquæducts conveying water to Italian cities and towns. I do not think he ever saw water flowing from his aquæduct, but I have. After freeing the attachments of the sheath of the facial nerve from the stylomastoid foramen, gentle traction will withdraw from the canal about $3\frac{1}{2}$ cms. of the nerve. This is followed at once by the escape of a stream of cerebrospinal fluid. (Fig. 6).

I propose to describe briefly to you with lantern illustrations a few points in certain investigations in which I feel sure the Master would have taken much interest:—

1. The regressive changes in the cells of the facial area of the left Rolandic cortex following experimental interference with the right facial nerve.

16. G. Fallopius—Omnia opera, p. 366, line 27.

2. The contractile tissue of the iris.
3. The culture of the cells of the embryo sciatic nerve.
   (a) In the egg.
   (b) In the subdural space.
   (c) By the ordinary method of tissue culture.
4. The ligation of arteries and the intimate process of the absorption of ligatures.
5. Double lateral implantation of the ends of a damaged nerve into the side of an intact neighbouring nerve.
6. The histology of incubated carcinomatous and normal tissues.

I.

The Regressive Changes in the Large Pyramid Cells of the Facial Area of the Left Rolandic Cortex, following Experimental Interference with the Right Facial Nerve.

The surgical interference with the trunk of the right facial nerve was either :—

(1) The grafting of the facial nerve to another nerve outside the skull.

(2) The substitution of a portion of the facial nerve by a portion of another nerve in the aquæduct of Fallopius.

(3) The removal of the trunk of the facial nerve outside the skull and of the facial nerve in the aquæduct of Fallopius.

The nerve-grafting operation in the Fallopian aquæduct was followed by much more rapid return of function in the facial muscles than when the facial nerve

was anastomosed to another nerve. It is probable that in the former case a living connection through the graft between the Rolandic cortex and the peripheral facial nerve was established long before there was any evidence of return of function in the facial muscles.

The question of how the brain cortex recovers control of the facial muscles is best understood by the study of other cases in which the conditions present are somewhat comparable :—When the speech centres of the left side of the brain are destroyed in early life the power of speech usually returns. We assume that the dormant centres on the right side of the brain acquire the function that would otherwise belong to the centres of the left cerebral cortex. In not one of our experiments did we observe contraction of any muscle on the right side of the face when the facial area of the right Rolandic cortex was exposed to Faradic stimulation.

The early regressive changes observed in the large pyramid cells were :— (Figs 7, 8, 9 and 10).

(1) The disappearance of the Nissl granules except at the base of the axon.

(2) Diminution of and alteration in shape of the body of the cell. The cell protoplasm becomes granular.

(3) Loss of the processes of the cells. The axon persists for a longer time than the other processes.

(4) The nucleus may assume an eccentric position.

The mechanism of the recovery of the function of the facial muscles is discussed in a separate paper.

II.

Observations on the Contractile Tissue of the Iris. [17]

This was the title of Lister's first contribution to the literature of science. The paper was printed in 1853. In 1848 Kölliker announced his discovery of the cellular constitution of all plain muscular tissue. Lister examined six human irides and those also of the rabbit, guinea pig and horse. He agrees with Kölliker that the sphincter fibres are readily seen, but that the dilator fibres are difficult of investigation. He believed that they consisted of narrow bundles which run inwards separately between the vessels, and are inserted into the border of the sphincter.

From my experience I can confirm Lister's statement. The radial fibres are difficult to demonstrate. The lantern slides are from preparations made from the iris of the horse and from the iris of the albino rabbit. They show the sphincter and radial muscles and the nerve supply of the iris. There are faint indications that the nerve supply of the plain muscular fibres of the iris is comparable to the nerve supply of the plain muscle fibres of the bronchi. Compare with the drawings in Larsell's [18] paper. (Figs. 11, 12, 13, 14, 15 and 16).

III.

The attempt has been made to cultivate the cells of the embryo sciatic nerve,

(a) In the egg.

(b) In the subdural space.

(c) By the ordinary methods of tissue culture.

These experiments were commenced in this College

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17. Quarterly Journal of Microscopical Science. Vol. I, 1853.

18. Journal of Comparative Neurology, 1921. "Nerve terminations in the lung of a rabbit," by O. Larsell, p. 105. See figure of distribution of nerve fibres to muscle bundles in the wall of an intrapulmonary bronchus. P. 121.

more than six years ago but were interrupted by my having to go to Australia.

(a) The egg experiments failed. Perhaps the method employed was faulty.

(b) Kanji Arai [19] of the University of Sendai, Japan, published a paper in 1928 with many illustrations describing the results of transplantation of portions of peripheral nerves into the brain, the spleen and the liver.

The following remarks concern only his transplants into brain tissue. The transplants were left for various periods of time in the brains, and were subjected then to microscopical examination. Professor Alexis Carrel in a letter to me, writes : " The article is not convincing because the nerves were transplanted into brains. If the same result could be obtained by tissue culture it would be very important." Nevertheless, the brain appears to be a suitable medium for peripheral nerve culture. There is no evidence that the brain tissue itself acted otherwise than as a culture medium. If there had been a growth of living elements, e.g., axis cylinders from the brain tissue into the transplant, how comes it that the transplant was after many days completely absorbed ? The embryo transplants in my experiments were placed in the subdural space so as to avoid any possible fallacy which might arise in consequence of the transplants being embedded in brain tissue.

Briefly, Kanji Arai's conclusions are as follows :— " After a preliminary degeneration, regeneration of the medullary sheaths occurs, the cells arranging themselves in rows and columns parallel to the axis of the fibres. The

19. Mitteil. u Allgemeine Pathologie u. Pathologische Anatomie, 1928. N. 345.

Schwann or neurilemma cells form fine fibres difficult to distinguish from nervous fibrillary elements. These fine fibres are apparently formed as differentiation products from the protoplasm of the cells. These cells also form a substance similar to myelin. The regeneration changes reach their acme in three months. The transplant then very slowly regresses and finally vanishes. The axis cylinders in the transplant in many places perish in two weeks, but sometimes remain for much longer in good condition. The axis cylinders may be observed for seventy days or longer embedded in the chains of Schwann cells. This must be considered a sign of life. In the seventy-day experiment I found numerous delicate axis cylinders and some pretty thick ones. They lay within the cell chains. No appearance of degeneration could be seen. These axis cylinders lying within the columns of Schwann cells I consider as newly formed, not as introductions from the surroundings."

The experiments on the transplantation of young nerves into the subdural space are only in the initial stages of investigation. I will describe one experiment, for it gives food for thought. Twenty-nine days after a fragment of the sciatic nerve of a young kitten had been implanted in the subdural space of a young adult cat it was removed and hardened and stained by the Ranson method. On examining the microscopical sections, no sign of the presence of axis cylinders was discovered; they had all disappeared. The fragment of nerve placed in the subdural space becomes adherent to the inner surface of the dura mater; it does not become adherent to the arachnoid. (Fig. 17).

While Kanji Arai found that when a nerve is embedded in brain tissue some of the axis cylinders persist for two or three months, the above experiment demonstrates that axis cylinders in the subdural space break up at once and are

absorbed. When a peripheral nerve is divided the fragmentation of the axis cylinders in the distal portion commences on the fourth day and the silver or other axis cylinder stains show no sign of their presence at the end of three weeks. It may perhaps be supposed that the brain tissue is a more favourable medium to prolong the life of the axis cylinder than is the cerebrospinal fluid in the subdural space which presumably contains the effete products of cerebral cell activity. It may be so, but this requires further investigation.

(c) Tissue Culture Experiments.*

These were conducted with the sciatic nerve of the fifteen to eighteen-day-old embryo chick. No response can be elicited on stimulating with the Faradic current the sciatic nerve or directly the muscles of the leg of the eleven-day-old embryo chick. On stimulating above the ankle of a fifteen-day-old embryo chick flexion and extension of the ankle and toes is observed, but on stimulating the sciatic nerve only a slight extension of the knee occurs. When a similar stimulation experiment is carried out with an eighteen-day-old embryo chick the muscular contractions are more pronounced. The result is the reverse of that obtained after suture of the sciatic nerve. In this case, some few months after the experimental operation, the main response is elicited by stimulation of the sciatic at or above the site of union and the muscular contractions become less and less as the stimulation proceeds towards the ankle, from the central to the peripheral region of the nerves. The phenomenon has been described by Durante as " phénomène de l'avalanche."

*Mr Steward has devised an eyepiece which is fitted to Model A, Cine Kodak, scientific model. This enables the observer to inspect the cells which are being filmed at any moment and be assured that the cells remain in focus. If any adjustment is required it can easily be done.

The cells seen in the film are of two kinds.

(a) **The Fibroblast** with a large oval nucleus and with processes extending in no determinate direction.

(b) **The Neurilemma** cell with a rod-shaped nucleus and two processes which extend a long distance in opposite directions. The processes imbricate with processes of other neurilemma cells. In this way long lines of cells are formed.

* * * * *

Under normal circumstances after the first differentiation of groups of cells in the embryo, each group of cells has a determinate hereditary tendency to spin a certain tissue and to spin that tissue only. Hence the fibroblast of the film spins fibrous tissue, while the neurilemma cells, if cultivated for a sufficient time and if not overwhelmed by the growth of the fibroblasts may be expected to give evidence of fulfilling their destiny by spinning sheaths.

The next lantern slides show the presence of myelin in the neurilemma cell. The Weigert method stains the nucleus black, and small discrete bodies in the cytoplasm are stained a dark colour. Some of the nuclei are unstained. The white substance of Schwann, which is not seen in these preparations, stains a pale blue-grey colour.

Figure 24—Shows a preparation made from the distal portion of the divided musculo-spiral nerve of the monkey. The nerve had been divided thirty days previously. Certain nuclei are stained black, and the cytoplasm contains darkly stained granules. In other cells neither the nucleus nor the granules in the cytoplasm are stained.

Figure 21 is a picture of a Weigert stained five day culture in vitro of the eighteen-day-old embryo-chick sciatic nerve. It is exactly comparable with the previous preparation. Some of the cells have taken the Weigert stain as described above and others are entirely unstained. Thus it is clear that there are two kinds of cells in the culture. The darkly stained nuclei of the three-day-old culture of the embryo-chick sciatic nerve are many less in number than in the five-day-old culture. It appears fair to assume that these cultures have grown cells which manufacture myelin. (Figs. 18, 19, 20, 21, 22, 23 and 24).

IV.

The Ligation of Arteries, and the Absorption of Ligatures by the Living Tissues.

On the 12th of December, 1867, Lister tied the common carotid of a horse with a silk ligature which had been steeped in a strong solution of carbolic acid. On the 31st of December, 1868, he tied the common carotid of a calf with a peritoneal ligature. This latter ligature, examined thirty days later, appeared on casual inspection still to be in place, but it was no longer the ligature that was visible encircling the artery, for by absorption and substitution it had been transformed into a band of living tissue continuous in structure with the arterial wall. As Lister explained, "the new tissue takes as a model the old, and forms at its expense, the old tissue is absorbed by the new, and as the old is absorbed, new is put down in its place." Lister continues, "The surgeon may now tie an arterial trunk in continuity close to a large branch, secure against secondary hæmorrhage. For my own part, I should now without hesitation undertake the ligation of the innominate

artery, believing that it would prove a very safe procedure." [20] (Figs. 25 and 26).

In conversation with me, Lister said that the ox-peritoneum ligature appealed to him as it was white fibrous tissue, a tissue corresponding in nature to that of the outer coat of an artery. Gold beater's skin is made from ox-peritoneum. Peritoneal ligatures can be made from gold beater's skin. In subsequent years Lister's energies were directed to the making of the catgut ligature (made from the intestine of the sheep) safe for surgical use, for many disasters had followed the use of catgut. [21]

When the calf was killed and the carotid artery at the site of ligation removed for examination, Lister's first impression was that the peritoneal ligature was still in being. The truth was that it had been perfectly absorbed and replaced by living tissue. This was demonstrated by teasing out the tissue with needles and submitting it to microscopical examination. The same deceptive appearance is shown in the lantern slide of ass carotids tied with kangaroo tendon ligatures. The next slide shows the absorption of the peritoneal ligature. The experiment was performed in 1888 at the instance of Professor Lister by my friend, the late Walter Edmunds and myself. I am glad of this opportunity of expressing my indebtedness in many ways to my friend Edmunds during the years in which we were associated together in arterial investigations. (Fig. 27).

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20. Lancet, April 3, 1869, and Brit. Med. Journal, Aug., 1871.

21. (a) See "System of Bacteriology," Medical Research Council, Vol. III, Chap. X, p. 319. Dr Bulloch records cases of tetanus following the use of catgut.
(b) "The Preparation of Catgut for Surgical Use." Special Reports —Medical Research Council. A fine historical review by Dr Bulloch. Cases of abscess, pyaemia, tetanus and anthrax following the use of catgut are mentioned.
(c) See Lancet, July 3, 1926, p. 11. Cases of Bryant, 1877; Callender, 1878; and Thomas Smith, 1887, showed catgut unreliable for tying great arteries in continuity. Lister strove continually from 1869 onwards to improve the preparation of catgut, so as to make it sterile, strong, supple and absorbable at the proper time.

The next slide shows some ligated horse carotids. It was these experimental ligations that gave me that confidence and certainty of success when the time came for me to tie the great arteries of man. When I was a dresser and also when I was a house surgeon in 1880, secondary hæmorrhage was rife in the wards of St Thomas' Hospital. Hence I determined as soon as the opportunity arose to work at the problem. In 1895 [22] the results up to date of ligation of the **first part of the subclavian artery** and of the **innominate artery** were published. The number of ligations of the first part of the subclavian artery was 15. The artery was first tied by Colles in 1813. Thirteen of the 15 cases died of secondary hæmorrhage, and the remaining two died of sepsis before the time at which secondary hæmorrhage was likely to occur. The number of ligations of the innominate artery was 22. This artery was first tied by Mott in 1818. Thirteen of the 22 cases died of secondary hæmorrhage, and seven of the cases from sepsis or cerebral complications. Coppinger's case recovered. In the case of Smyth, of New Orleans, hæmorrhage took place on the 15th, 33rd, and 55th days. On the 55th day the bleeding was finally arrested by tying the vertebral artery and filling the wound with shot. It is not possible for me to express in words the impression produced on the mind of a young surgeon by these appalling tables. And yet Joseph Lister had pointed out the way to success in 1869, and I and other surgeons have in the fullness of time proved the truth of his statements by the successful ligation of the great arteries of man. (Figs. 28 and 29).

In 1920 the late Professor Perthes [23] of Tubingen showed how great arteries could be obstructed without

22. Erichson—Science and Art of Surgery, 1895, Vol. II., pp. 192-195.

23. Langenbeck's Archiv. 1920.

injury to the intima. The ligature employed was a broad piece of fascia and a portion of the same tissue was folded and placed under the region of the knot. This appears like a return to an ancient practice, for many of the great surgeons of the past used similar or other means to avoid injury to the arterial coats. Among these may be mentioned[24] Ambroise Paré (1570), Alexander Monro (1725), Heister (1718), Platner (1758), Guattani (1772), Buzani (1770), Benjamin Bell (1787), John Hunter (1785), Antonio Scarpa (1805), and Sir Charles Bell (1821). Surgery has been said to move in circles, but this is not true. Sir Michael Foster[25] in a paper on "The Coagulation of the Blood" in 1864, wrote, "Here, as in so many other fields, we seem after many wanderings to come back to an old faith. Seem but only seem. The mind of man moves not in circles but in spirals. Our faces may be again looking towards the same point of the compass, but we are on a higher level and with a wider horizon." (Fig. 30).

My friend Walter Edmunds, and myself, devised a knot for tying the great arteries in continuity. The object was to prevent the giving way of the first hitch of the reef knot, in consequence of the pressure of the blood and the elastic resilience of the arterial wall, before the second hitch was tied. In the 'eighties of the 19th century, cases of ligation in continuity were reported in which, after ligation, the artery was discovered to be patent at the site of ligature. Nicholas Senn[26] about the same time, or shortly before, invented a method of using two ligatures for ligating the arteries in continuity. In the correspondence which followed I maintained the superiority of our knot, but whether Senn was convinced by the argument, I never learned. I

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24. See "Ligation in Continuity," p. 353 et seq.
25. Nat. Hist. Review, 2nd Series, p. 180.
26. "Ligation in Continuity," p. 393.

may add that the "stay-knot" has never failed me. I used it in the Great War for ligating the first part of the left subclavian artery [27]; perhaps the most difficult operation which I have ever had to perform.

The intimate process of the absorption of the peritoneal ligature.

In some Ziegler chamber experiments conducted with Charles Sherrington in 1887 [28] we were able to observe the digestion of leucocytes and red corpuscles in the food vacuoles of the wandering connective tissue cells. These cells may be looked upon as a hothouse variety of amœba. The explanation of the appearances we observed was illuminated by papers in the Journal of Physiology by Miss Greenwood [29] on digestion in amœba proteus and actinospherium. Little Monads Euglenoe and Algæ co-existing in the same water were ingested. A fluid medium in the food vacuole of the amœba appears essential for the manifestation of primitive digestive activity. Unshielded, uncoagulated proteid matter is the food of perfection for either the connective tissue cell or amœba proteus. Clearly a proteolytic ferment is secreted into the food vacuoles of these living cells. But what is of equal importance is that Miss Greenwood observed that Monads that came to rest against the protoplasm of amœba proteus became inert and dead, and were apparently acted on by the same agent as was present in the food vacuole.

This explains what happens in the absorption of organic material such as catgut, peritoneal ligature or blood clot. All parts of the foreign body are not taken into the food vacuoles of the invading cells, but are disintegrated by the proteolytic ferment secreted from their surface. (Figs. 31, 32, 33, 34, 35, 36, 37 and 38).

27. Journal of the Royal Army Medical Corps, 1918. Vol. XXXI., p. 417.
28. Journal of Physiology, 1889.
29. Journal of Physiology, 1886 and 1887.

V.

Double Lateral Implantation of the Ends of a Damaged Nerve into the Side of a Neighbouring Intact Nerve.

During the Great War many instances came to my notice in which a nerve was destroyed for a considerable distance, while a neighbouring nerve was undamaged. The arm, the forearm, the popliteal space and the brachial plexus were the sites of these injuries. The ends of the destroyed nerves could not be brought together. They were united end to side to a neighbouring intact nerve. The part of the intact nerve between the anastomoses acted as a living graft. These operations were successful when after treatment—movement of joints, massage, &c.—was carried out intelligently for a long period. [30]

When the War ended I was anxious to see what actually happened in these cases, and how recovery occurred. By the kindness of the Medical Research Council I was able to do so.

I believe this operation will become of much importance in the surgery of the nerves in the coming years, both in civil and military surgery. It is clearly of more advantage to employ a living nerve as a graft than to transfer a portion of nerve from some other region of the body and to inveigle it into position between the two ends of a divided nerve. (Figs. 39, 40 and 41).

VI.

The Histology of Sterile Incubated Carcinomatous and Healthy Tissue.

When I returned from Germany in 1885, Professor

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30. "Some Results of Nerve Anastomosis." British Journal of Surgery, Vol. XI., p. 327, 1923-24. "Further Results of Nerve Anastomosis." Vol. XIII., p. 533, 1925, 1926.

Shattock and I decided to work on the problem of the intimate pathology of malignant disease. As a side issue of this investigation we incubated pieces of carcinoma and made a number of control experiments with healthy tissue. Portions of more than forty carcinomatous tumours were incubated, and a large number of similar experiments were made with healthy tissues.

The incubation periods lasted from seven to thirty-three days.

The appearances observed in the carcinomatous cell.

" The outline of the cell protoplasm is not visible. The nuclei are granular, the nuclear matrix between the granules being slightly stained or colourless. A delicate continuous outline exists to all the nuclei. Many of the nuclei have a spinous border due to the projection of granules from it, the limit of the nucleus being clearly defined. In other instances the granules have passed beyond the proper margin of the nucleus, an extremely delicate thread-like process or stalk still connecting the granule with the boundary of the nucleus. The granules vary in size on leaving the cell-nuclei. They are mostly spheroidal, and in many instances oval or comma-shaped, or with a delicate filament or tail. In some of the nuclei one or two granules remain attached to the nucleus by a delicate process, the nucleus itself being scarcely distinguishable. The explanation of this last appearance may be that the granules have all passed out of the nucleus. Similar granules occur here and there free in the loculi. In the process of fertilisation, the head of the spermatozoon penetrates the ovum cell, and enlarges to constitute the male pro-nucleus. After the fusion of the male and female pro-nuclei the process of segmentation

commences. The above described appearances of the incubated carcinomatous cell may possibly indicate the working of a sexual process. The extrusion of the chromatin granules may prepare the nucleus and cell for sub-division, whilst the extruded particles may represent the male elements of such cells, and incite division in others after the manner of a spermatozoon. Should this prove to be so, the extruded particles might be regarded as cancer-sperm and be named carcinozoa." [31]

The appearances observed in incubated normal mammary epithelial cells, and in the incubated epithelial cells of many other organs other than the mamma.

The cells of normal tissues when incubated do not exhibit any sign of the granules which are seen under similar circumstances in the carcinomatous cell. I have always intended to repeat these experiments, but up to the present time I have not found the time to do so. Meanwhile the real meaning of the appearances seen in the sterile incubated carcinomatous cell is unknown. (Figs. 42, 43 and 44).

Pieces of incubated carcinoma, when implanted in the tissues of a living animal do not infect the animal with the disease. The method of transmission in infective diseases is not always so direct as such grafting experiments presuppose. The negative result does not disprove in the case of carcinoma the presence of an infective agent but only that the method employed to demonstrate it was unsuitable. The result in some ways is comparable to the failure to transmit malaria to a healthy bird by the injection of blood containing the hæmatozoon from a malarious bird. Professor Shattock and I found, too, that it was not possible

31. Trans. Path. Soc., 1888.

to cause experimental infection of a rabbit by intravenous injection of the psorospermial bodies so common in the rabbit's liver. But the carcinoma transplantation experiments introduced another factor. It was an attempt to transplant carcinoma from man to an animal of another species. We now know that this cannot be successfully accomplished.

I have not any knowledge of the real meaning of this migration of the chromatiniferous granules from the nucleus of the carcinomatous cell. Perhaps it is fortunate that there is no time to discuss the problem, for I might be led into making a guess which has no experimental foundation.

CONCLUSION.

Mr President,

This lecture is rapidly drawing to a close. In the short time allotted to me it is only possible to salute but a fragment of the important events in the life of my illustrious Master. But this is of no moment—Joseph Lister is not,

"A precious friend hid in death's dateless night." [32] He dwells among us, enshrined in everlasting remembrance. in all that is most beautiful in our art and science.

* * * * *

So

"When to the sessions of sweet silent thought
I summon up remembrance of things past."

* * * * *

"And if the while I think of thee, dear friend,
All losses are restored, and sorrows end." [33]

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32. Shakespeare — Sonnet, "Remembrance."

33. Shakespeare — Sonnet, "Remembrance."

Fig. 1—Laurelwood.

The country home of Dr and Mrs Arthur B. Duel, 75 miles from New York City. The house is situated on the edge of a primeval forest. The country around consists of low hills, valleys, woods, lakes and streams. The ground is rock. The trees of the forest have their roots deep down in the fissures of the rock. From every rock a trickle of water flows. Laurelwood is some 1800 feet above the level of New York City. Eagles nest on the cliff edge of the lake, which is situated some hundreds of feet above the house.

Fig. 2 — The Surgical Research Laboratory built by Dr Duel.

The laboratory is some 800 yards from the house, and is concealed from it by a fold in the ground. Besides the large indoor and out-of-door cages there is a modern operating theatre, a sterilising room, a theatre sister's room, a surgeon's room with shower bath, a kitchen, a photographic room and several store-rooms.

The temperature in winter of the inside cages was maintained at from 73-75 degree F. Ultra-violet light was installed. The baboon cages were kept scrupulously clean. The food was always fresh and the milk sterilised. Cod liver oil and lump sugar was in the daily menu.

Fig. 3—" Old Bill " yawning.

In each of these baboons a fresh nerve graft was substituted for a portion of the right facial nerve in the aquæduct of Fallopius. In both cases complete recovery from right facial palsy took place.

Fig. 4 —The " MacNab."

The final examination of Old Bill was carried out 598 days after the operation. The final examination of the MacNab was carried out 613 days after the operation.

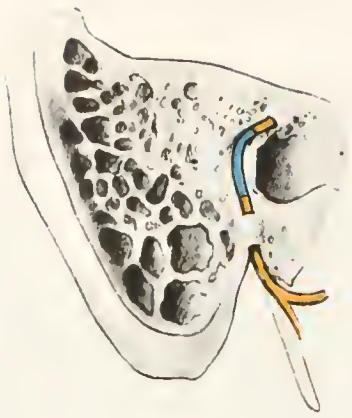


Fig. 5—Type of operation which was performed in the experiments on Old Bill and The MacNab.

The part of the nerve coloured blue represents a fresh nerve graft which has been substituted for a portion of facial nerve.

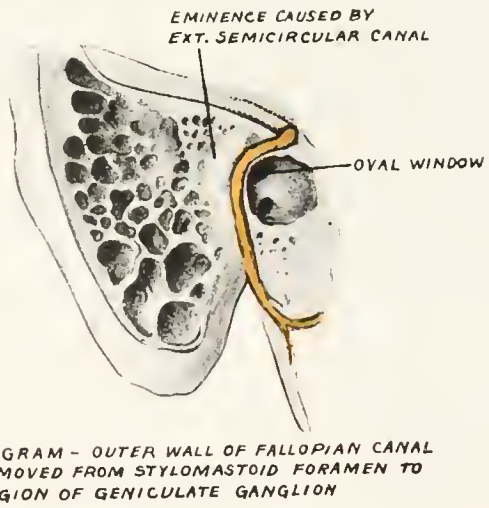


Fig. 6—When the attachment of the sheath of the facial nerve to the stylomastoid foramen is freed, gentle traction on the nerve will cause it to come away. This is followed by the escape of cerebro-spinal fluid. The rupture of the nerve takes place in the internal auditory meatus, or it may be avulsed from the lower margin of the pons.

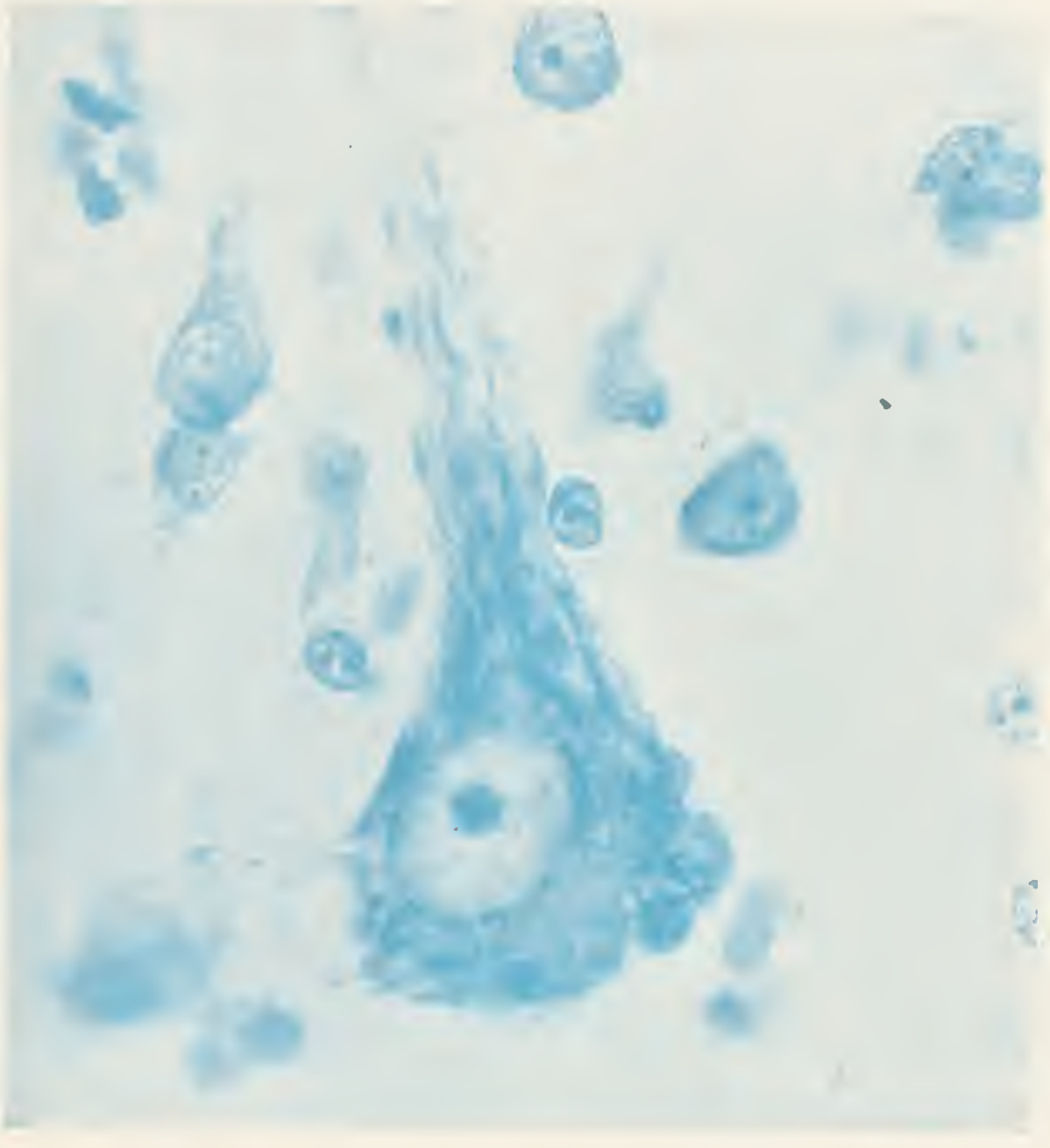


Fig 7—Baboon—Facial area of right Rolandic cortex 356 days after operation in which a superior laryngeal-facial anastomosis was done on the right side.—Nissl methylene blue stain.

Large pyramid cell with Nissl granules. The cell is well stained and of normal appearance.

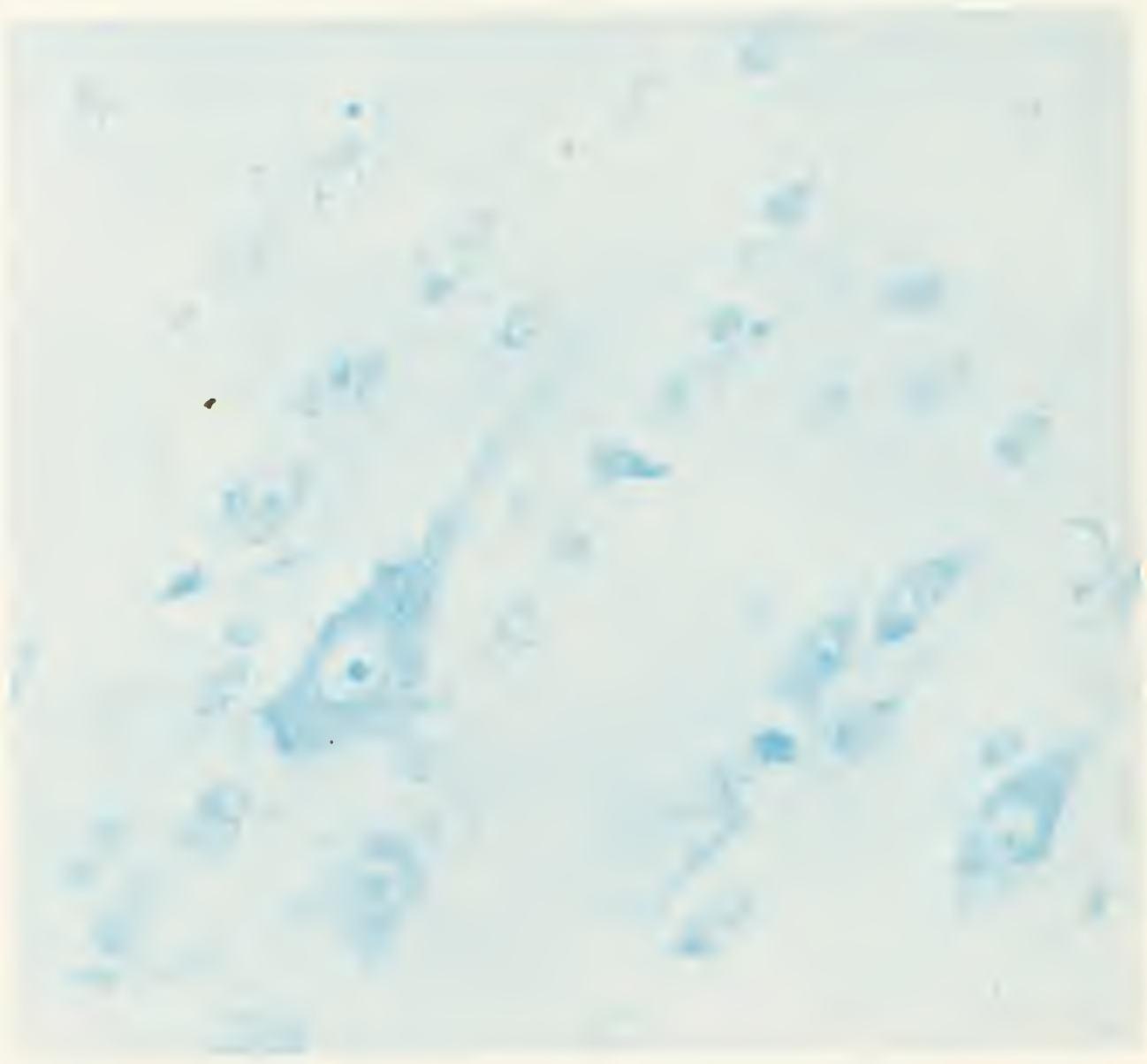


Fig. 8—Baboon—Facial area of left Rolandic cortex, 356 days after operation in which a superior laryngeal-facial anastomosis was done on the right side.—Nissl methylene blue stain.

The recovery from right facial palsy was imperfect. The lower lip muscles and risorius responded well to the Faradic current, but the response of the upper lip muscles was poor.

The sections are very faintly stained. The number of cells is much less than on the right side. A pyramid cell faintly stained is seen with a long axon. At the base of the axon Nissl granules are visible. The body of the cell is diminished in size and the protoplasm is granular in appearance.

Fig. 9—Baboon—Facial area of left Rolandic cortex.—9 mm. of the facial nerve was replaced by 9 mm. of the nerve of Bell in the Fallopian aquæduct on the right side. Specimen obtained 406 days after the performance of the operation.— Nissl methylene blue stain.

The right facial palsy was completely recovered from: the electrical reactions of the muscles of the right face were normal.

The figure shows a large pyramid cell faintly stained and with numerous Nissl granules. Notwithstanding the perfection of the physiological recovery the cells still take the stain faintly. Is this a stage in the evolution of anatomical recovery?

Fig. 10—Rhesus Monkey—Facial area of left Rolandic cortex 50 days after the removal of the trunk of the right facial nerve outside the skull and in the Fallopian aquæduct.

The section shows advanced cellular degeneration. The cell near the centre of the field, with a swollen nucleus which has no nucleolus, is the remains of a large pyramid cell. The cytoplasm remains as a ring around the nucleus. The shortened axon is visible.

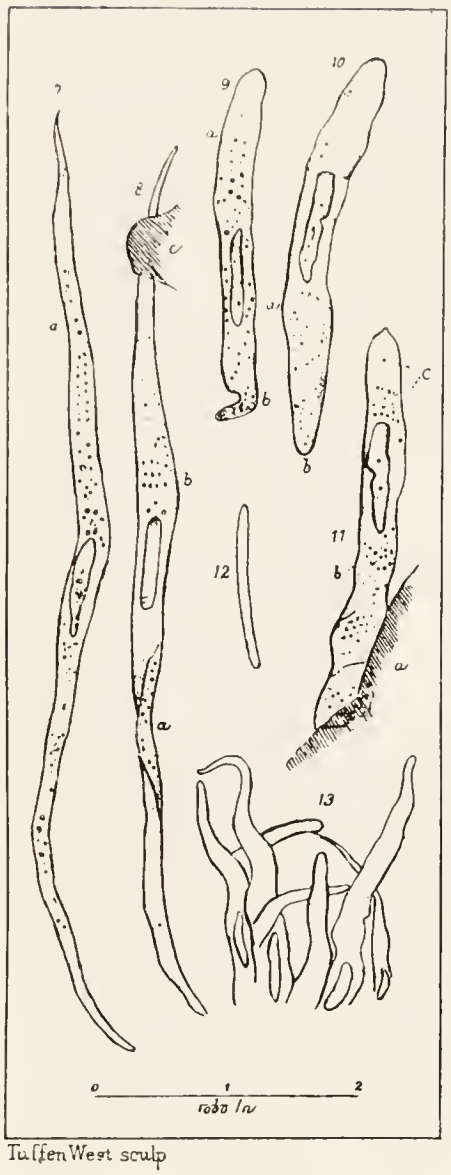


Fig. 11 — Plain muscle fibre-cells of the human iris. —Lister.

Fig. 12—The iris of the eye of a horse.

The tissue containing the sphincter pupillæ is clearly seen. The radiating bands which extend from the periphery to the sphincter are made up of much connective tissue, pigment, and narrow strips of the dilator pupillæ muscle. Between the bands lie the arteries and nerves. The mass of pigment at the back of the iris of the horse can easily be removed by scraping, but even then the amount of pigment scattered through the tissue of the iris spoils the section for the study of muscle and nerve.

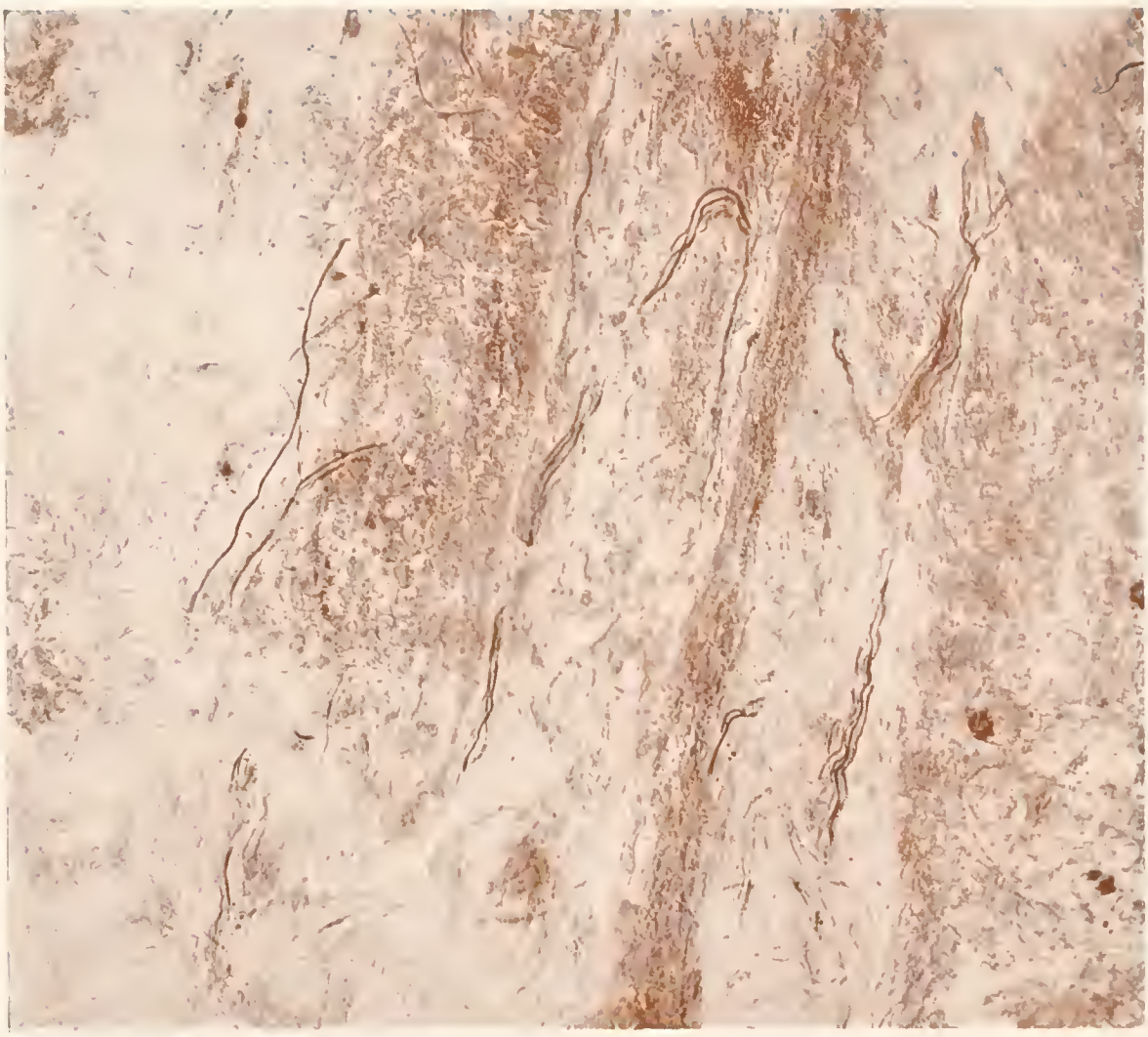


Fig. 13—Radial muscular fibres of the dilator pupillæ of the albino rabbit.

The nerves run in a radial manner between the narrow bands of muscle from the periphery of the iris to the sphincter pupillæ.

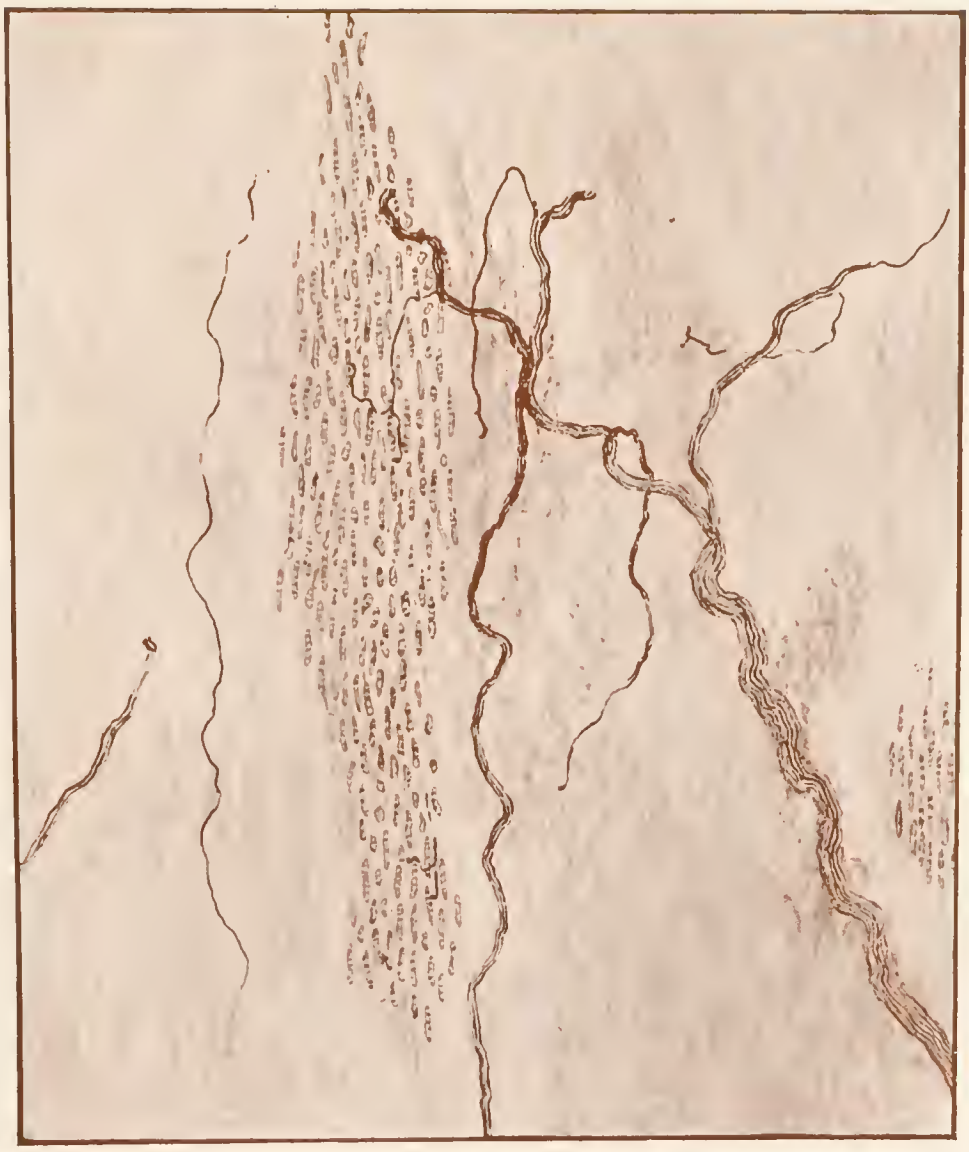


Fig. 14—Radial muscular fibres and nerves of the iris of an albino rabbit.—Ranson stain.

Fig. 15—Radial muscular fibres of the iris of an albino rabbit.—Van Gieson stain.

Fig. 16—Nerves of the iris of the albino rabbit. — Methylene blue—intra vitam stain.

Dimly seen at the lower part of the figure are the muscular fibres of the sphincter pupillæ.

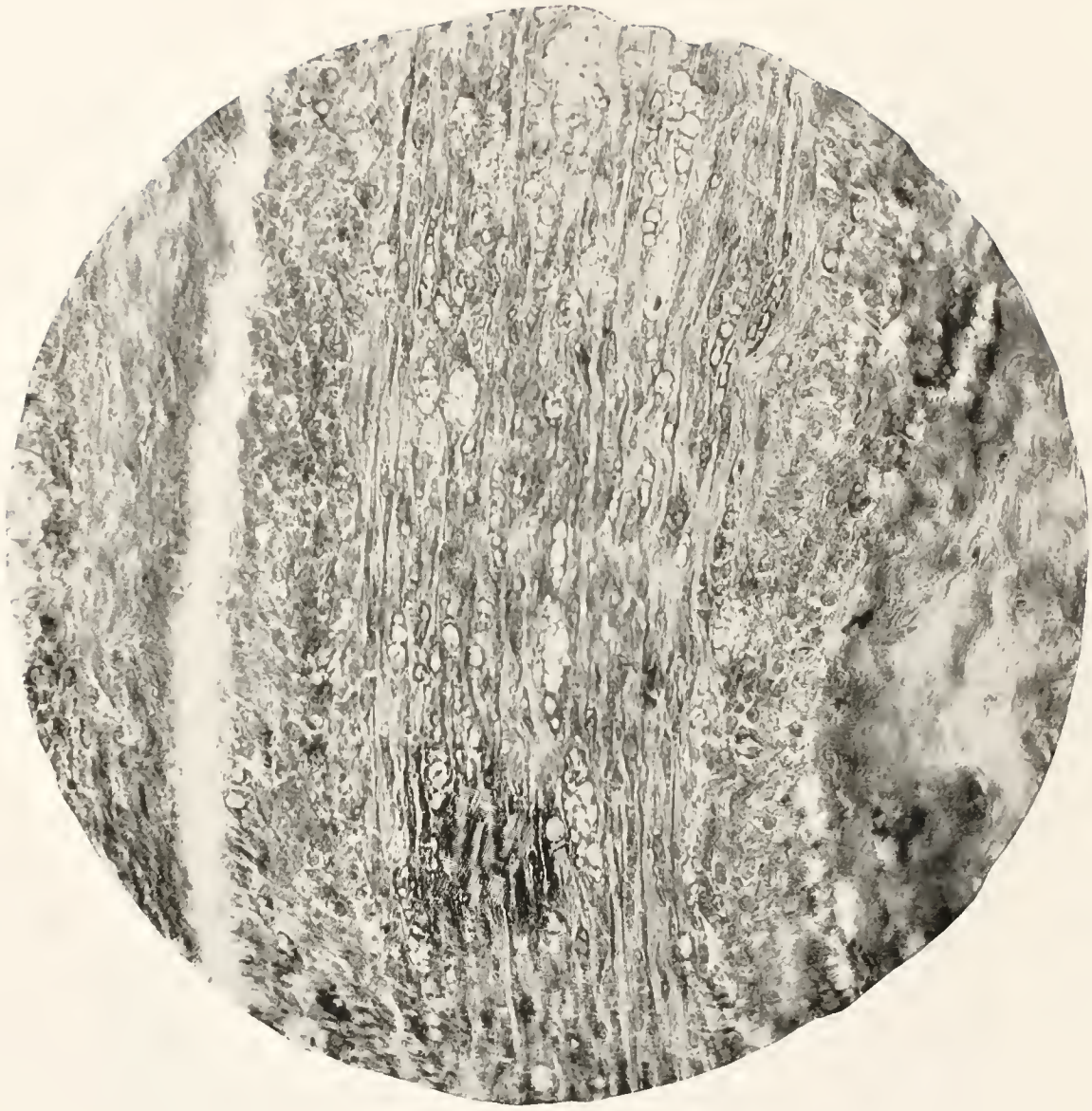


Fig. 17—Sciatic nerve of a young kitten which had been for 29 days in the subdural space of an adult cat.—Ranson stain.

All trace of the axis cylinders has disappeared. The medullary sheaths are broken up and are in process of absorption.

Long lines of cells with rod-shaped nuclei are visible. Their processes join or imbricate with the processes of adjoining cells. The activity of the neurilemma cells indicates that this fragment of sciatic nerve is not a dead structure.

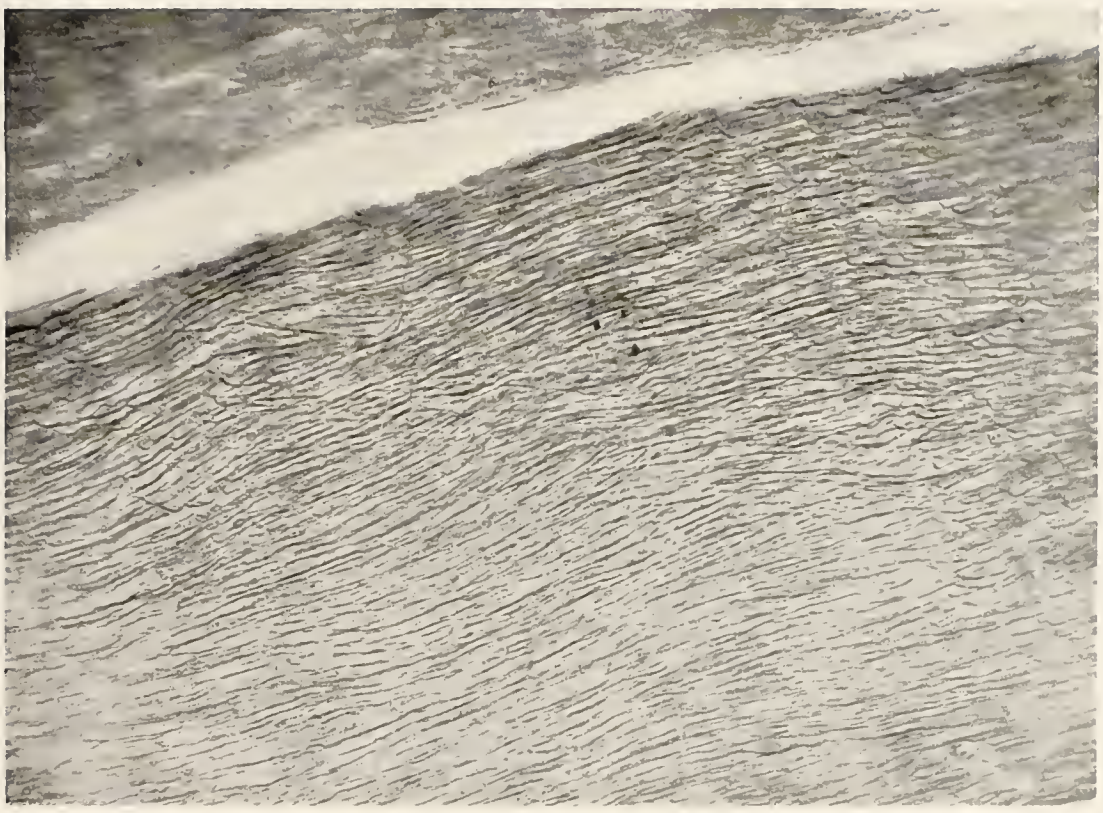


Fig. 18—Portion of the sciatic nerve of an eighteen-day-old embryo chick.—Ranson stain—x 850. Under a Zeiss D lens, Ocular 4, the axis cylinders appear as extremely fine dark lines.

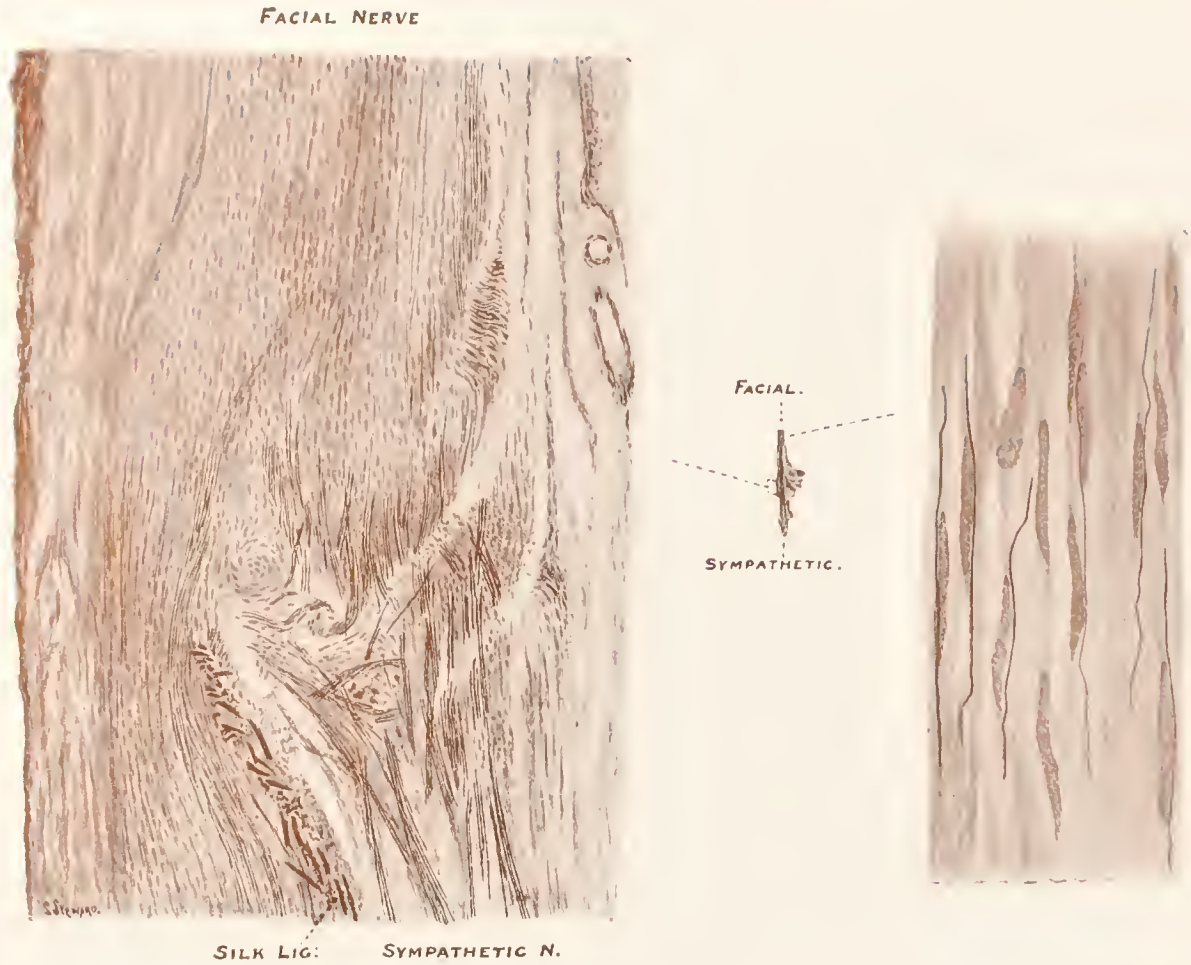


Fig. 19—Cervical sympathetic-facial anastomosis.—Cajal stain. Fifty days (x 150).

A multitude of neurilemma cells are present, arranged longitudinally. Nuclei rod-shaped. Fine dark lines are seen running by the side of the nuclei. These dark lines are either continuous or discontinuous. At the anastomosis a piece of unabsorbed silk ligature is visible, and here can be seen many oval nuclei of connective tissue cells. In the high power drawing (x 1000) are seen discontinuous black lines lying in the protoplasm of the cells, close to the nuclei. The imbricating ends of discontinuous fibres in some instances appear to have become fused together and to have formed long dark continuous lines.

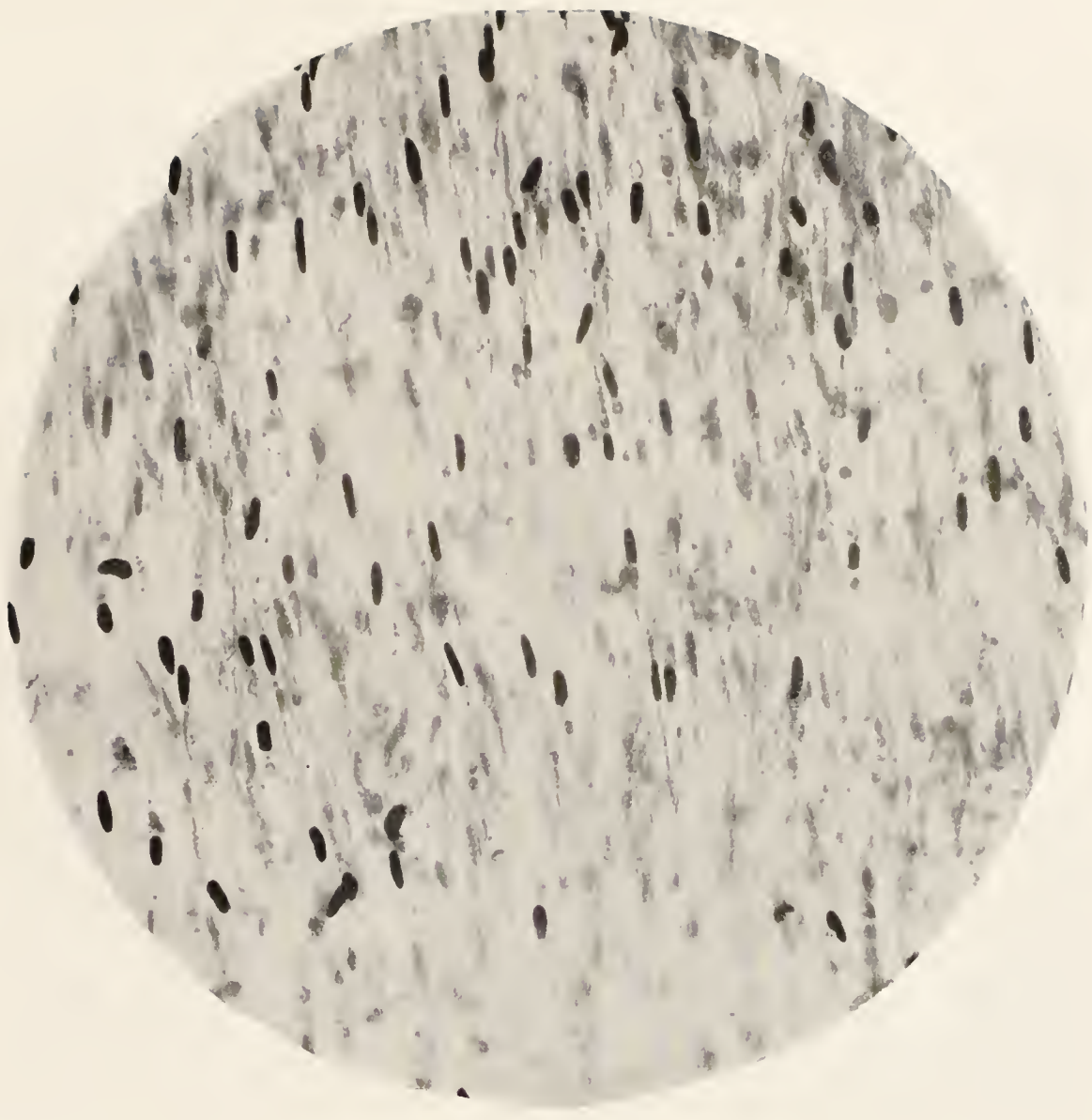


Fig. 20—Sixty-hour culture in vitro of an 18-day-old sciatic nerve of the embryo chick—Weigert stain.

The nuclei of some cells are stained and others are unstained. The stained nuclei are less in number than the unstained. There are some connective tissue cells containing stained fragments of myelin. There is a faint indication of a longitudinal grouping of the cells. In a 24-hour culture stained by the Weigert method, the stained nuclei seem to be many less in number than in the 60-hour culture. The cells are spreading in all directions and there is no indication of longitudinal grouping. Whether the nuclei of the young neurilemma cells take the Weigert stain at once or acquire later the capacity to do so is difficult to determine.

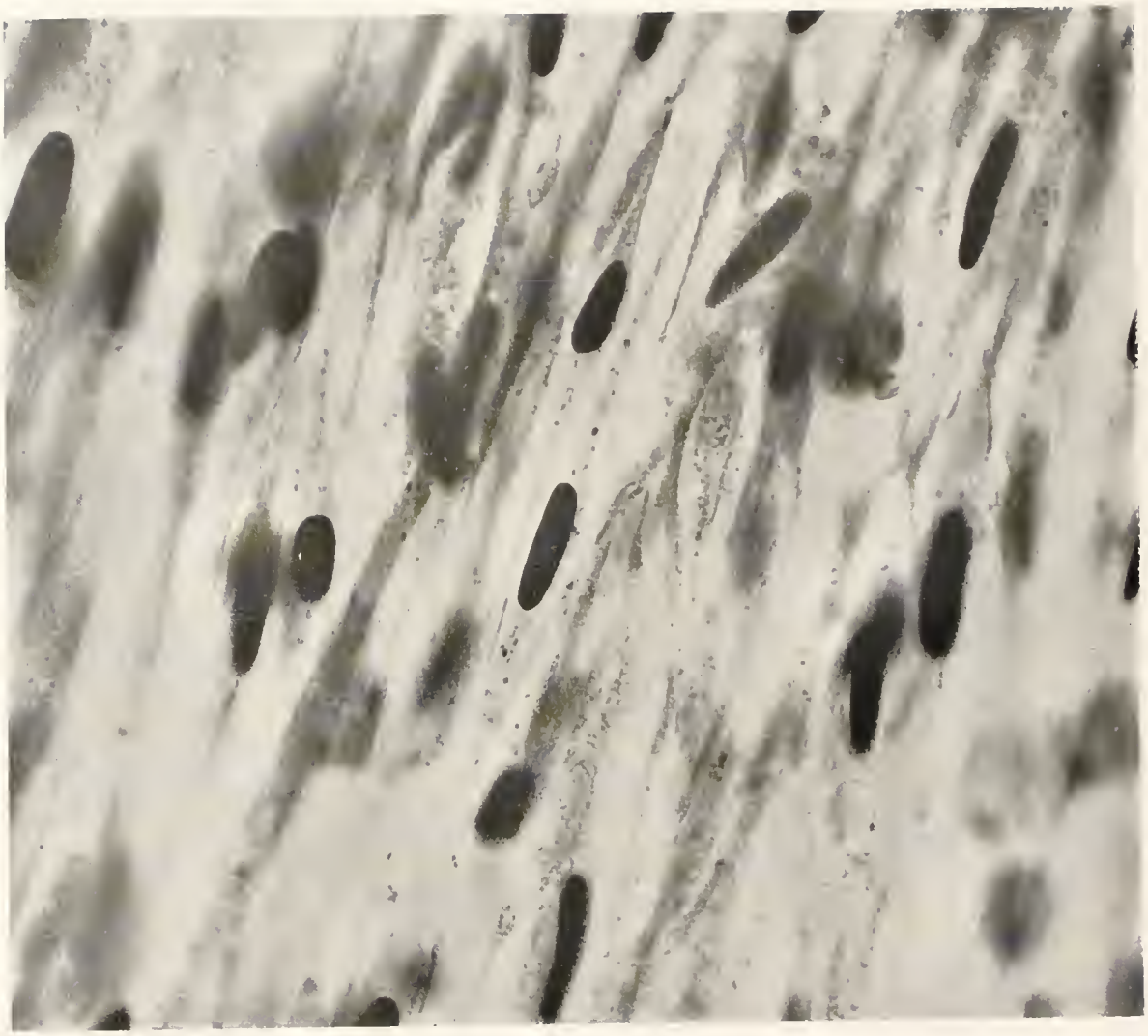


Fig. 21—Five-day culture in vitro of the sciatic nerve of an 18-day-old embryo chick.—Weigert stain.

The cells are arranged in long lines which seem to predicate the formation of a definite tissue. The cell in the centre of the picture shows a stained rod-shaped nucleus and stained granules in the cytoplasm. The number of stained nuclei appear to be more numerous than in the 60-hour culture.

Fig. 22—Drawing of a connective tissue cell (fibroblast) seen in the film shown at the lecture.

Note, the oval nucleus, the outline of which was in constant movement, also the many processes of the cell.

Fig. 23—Drawing of a neurilemma cell seen in the film shown at the lecture.

Note the rod-shaped nucleus and the two processes. The neurilemma cells form long lines; their processes imbricating with those of adjoining cells.

Fig. 24—Section of the distal segment of the musculo-spiral nerve of the monkey, which had been divided and not sutured 30 days previously.—Weigert stain.

A.A.—Neurilemma cells, the nuclei of which have taken the stain well. Small stained particles are visible in the cytoplasm.

Some nuclei are unstained; others show a deposit of myelin as small discrete bodies.

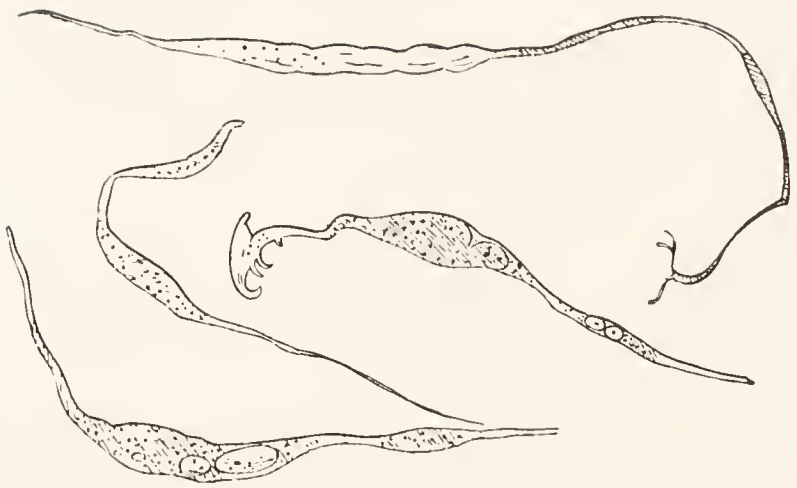


Fig. 25—Living cells which have replaced the peritoneal ligature (x 500).—Lister.

On microscopical examination the substitution of the ligature material by connective tissue is seen in various stages. In places there is a well-developed fibrous tissue. In others, where a minute fragment of ligature is still unabsorbed, the tissue around is cellular. Absorption of a foreign body must be complete before the tissue cells in the neighbourhood attain perfection.

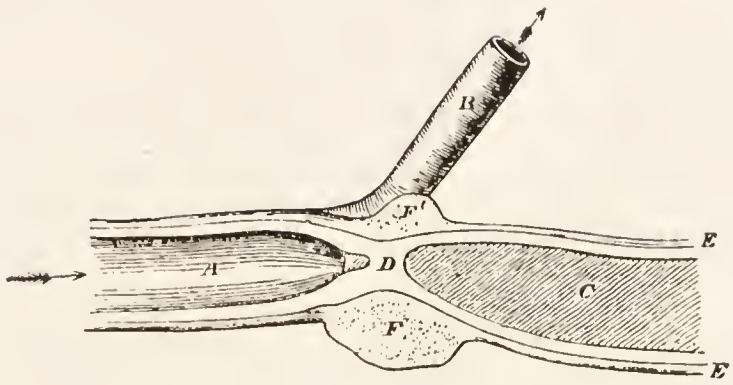


Fig. 26—Ligation of the carotid artery of the calf with ox-peritoneal ligature (x 3).—Lister.

The artery (A) is free of clot on the cardiac side of the ligature. On the distal side a coagulum (C) fills the artery. When the knot of the ligature was completed it is probable that the coats were not in contact. The ligature was applied near a large collateral branch. The peritoneal ligature (F), has been almost entirely absorbed and replaced by living tissue.

Fig. 27—Transverse section of an ox-peritoneal ligature after being for 55 days around the carotid of a horse. The spaces between the folds into which the membrane was thrown in manufacture are seen as white streaks. It is along these, that on the side away from the artery that the cellular invasion is occurring.

Fig. 28—Ligation of the carotid artery of the horse, 3/5ths of natural size.—(Plate 1 from " Ligation in Continuity ").

1.—Common carotid of horse, 24 hours after ligation. Two kangaroo tendons. Stay-knot. Coats uninjured. Lumen occluded. Clot fell out on section. Intima in apposition for 4 mm.

2.—Common carotid of horse, 14 days after ligation. Two floss-silk ligatures. Stay-knot. Coats uninjured. Intima in apposition for 3 mm.

3.—Common carotid of a horse, 21 days after ligation. Two kangaroo tendons. Stay-knot. Coats uninjured. Lumen occluded. Intima in apposition for 2.5 mm.

4.—Common carotid of horse, 14 days after ligation. Three kangaroo tendons. Stay-knot. Coats uninjured. Lumen occluded. Intima in apposition for 5 mm.

5.—Common carotid of horse, 21 days after ligation. Three silkworm-gut ligatures. Stay-knot. Coats uninjured. Lumen occluded. Intima in apposition for 4.5 mm.

Fig. 29—Ligation of the innominate artery for innominate aneurism.—R.C.S. Museum 5444. British Journal of Surgery, Vol. IX.

The operation was done on December 31, 1918. The patient died on June 6, 1921, of cardiac and renal disease. The aneurism was cured. The distal portion of the innominate is slightly enlarged and changed into a fibrous mass. The ligation was effected by means of a stay-knot. The artery is obstructed at the site of ligature.

A.—Diagram showing the occlusion of the artery.

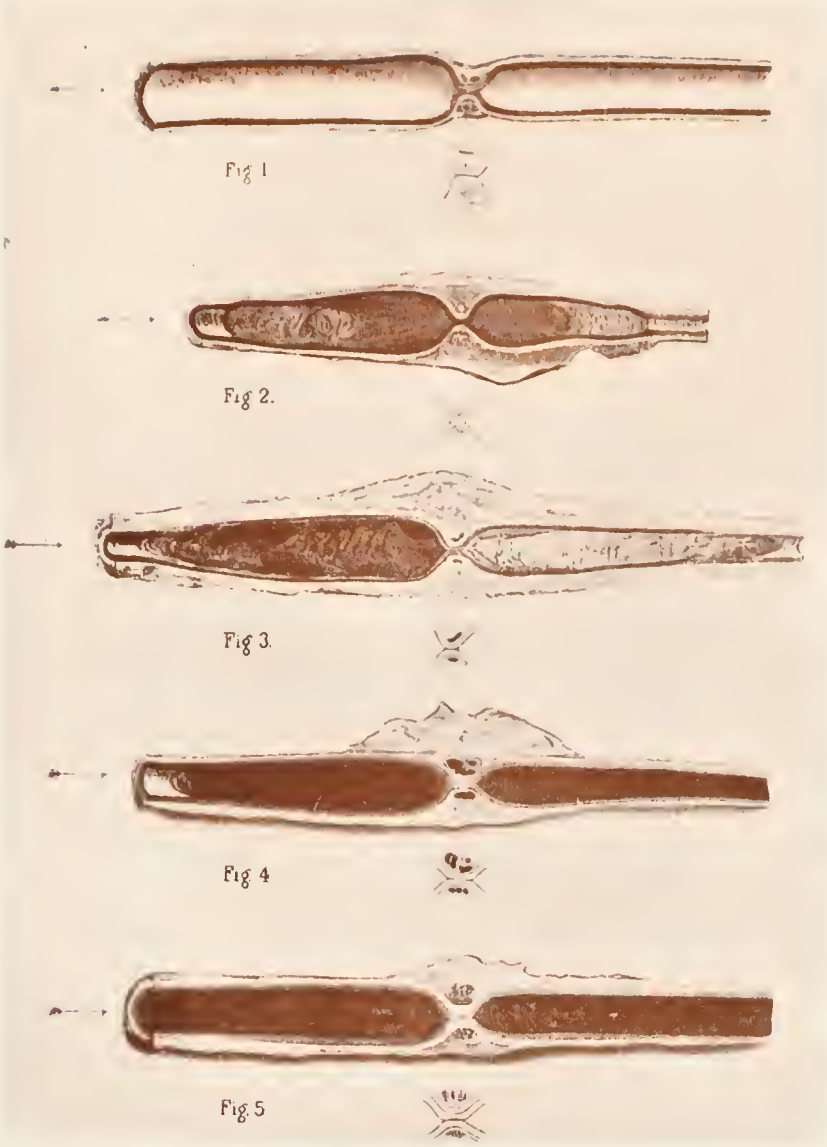


Fig. 28.

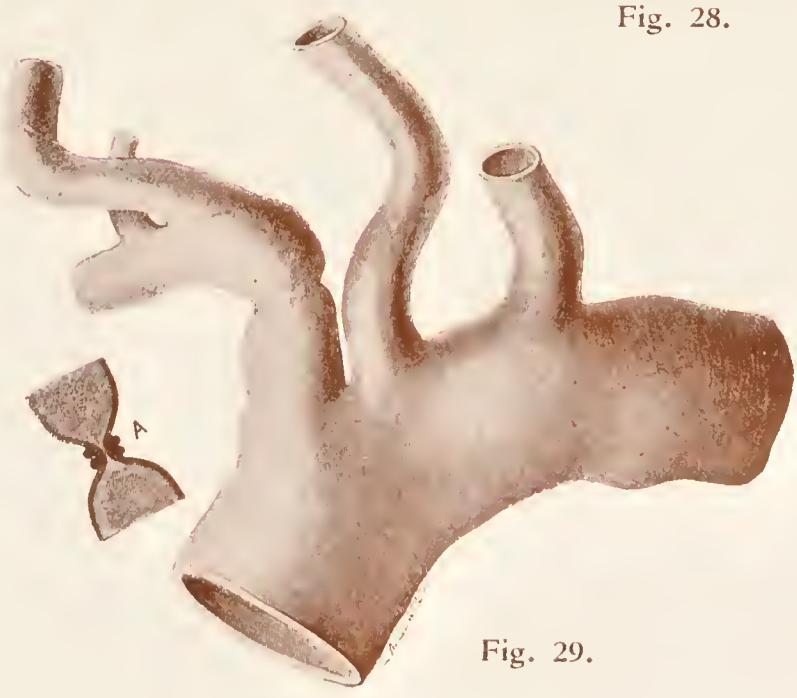


Fig. 29.

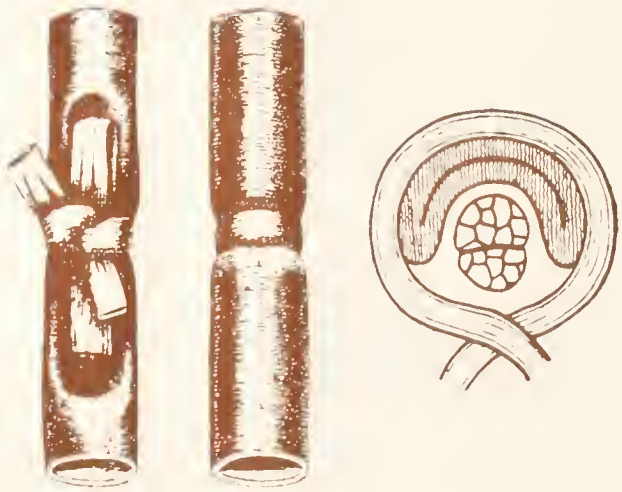


Fig. 30—The method of Perthes, of Tubingen (1920), designed to occlude a great artery without injury to the intima.

The ligature employed was a broad piece of fascia and a portion of the same tissue was folded and placed under the region of the knot.

Fig. 31—Amœba Proteus and Actinosphœrium.

A.—**Amœba Proteus**—Infusoria and Algæ undergoing digestion in vacuoles.

B.—**Part of an Amœba Proteus**—Large vacuole in which lies a Stylonchia undergoing digestion.

C.—**Part of an Amœba Proteus**—Infusoria and Monads lying in digestive vacuoles.

D.—**Actinosphœrium**—Many digestive vacuoles containing Euglenœ in various stages of digestion.

Fig. 32—Absorption of ox-peritoneum ligature by living cells.—Hæmatoxylin and Eosin.

A.—A giant cell containing in its protoplasm a fragment of ox-peritoneum ligature—x 750. (13 weeks.) The protoplasm is in close contact with the fragment of ligature. Several light areas cross the fragment where absorption has taken place. They may contain the ferment in a fluid medium. All trace of the fibrous structure of the ligature has been lost.

B.—A cell with many small fragments of partly dissolved ligature in its protoplasm—x 1100. (9 weeks.) There is no food vacuole visible; possibly its labours are completed and the debris of the digestive process has been shed into the surrounding protoplasm.

C.—A cell in the protoplasm of which can be seen a food vacuole containing the remains of a fragment of ligature —x 1100. (9 weeks). Around the fragment is a clear space containing fluid and presumably a proteolytic ferment.

D.—A cell in the protoplasm of which are two food vacuoles. In each vacuole is a fragment of ligature as yet not completely digested. Around each fragment is a clear space containing fluid and presumably a proteolytic ferment—x 1100. (9 weeks.)

Fig. 33—The absorption of Lister's ox-peritoneum ligature (after 9 weeks). The fragments of ligature are encapsuled. Encapsulation is a stage in the process of absorption. A multinucleated cell is visible towards the right of the figure. The fragments of ligature are surrounded by what appear to be empty spaces; but this is not so. The spaces contain fluid, and presumably a proteolytic ferment. The fragments of ligature show no sign of structure.

Fig. 32.

Fig. 33. ×750

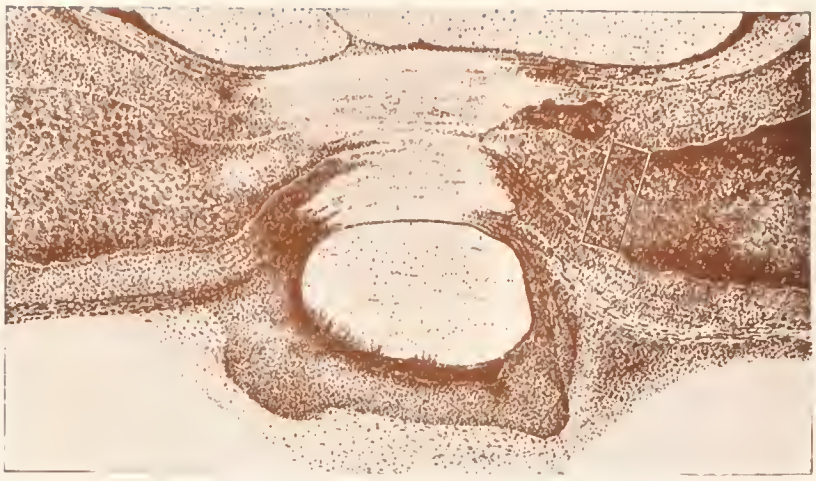
Fig. 34—Ziegler chamber experiments.

1.—Experimental chamber 72 hours in the peritoneal cavity of a rabbit. Large amœboid plasma cells attacking altered red corpuscles and dead leucocytes. Prepared over osmic vapour.

2.—Close to the opening of the same chamber. Five large wandering connective tissue cells. One of them contains a leucocyte within a large vacuole.

Fig. 35—Cracks and fissures of the clot (x 90).

The drawing was made from a portion of clot in the carotid artery of a horse 14 days after ligation. It was taken four inches from the site of ligature where the clot was not adherent to the arterial wall. The outline of the red cells is distinct. Although the ligation had taken place 14 days previously, this portion of clot is of much more recent date.



X 26

X 160

Fig. 36—Carotid artery of a sheep 21 days after ligation with Kangaroo tendon.

The upper figure (x 26) shows that the coats of the vessel are uninjured; the intimæ of opposite sides being in opposition. The fenestrated coat of Henle appears as a white line. The part enclosed in white lines is represented more highly magnified in the lower figure. In the **lower figure** (x 160), the tunica intima is greatly thickened, solid columns of cells have passed from the endothelium of one side to that of the opposite side, through the substance of the coagulum, which is mapped out into districts. The outlines of the red corpuscles are no longer visible. The districts are filled with a yellow granular material. The change in the clot is due to the action of a ferment secreted by the invading cells, and is a stage in the process of absorption and substitution of the clot by the living cells.

Fig. 37—Two carotids of the Ass, ligated with Kangaroo tendon.

The left hand artery is 77 days after ligation. The right hand artery is 67 days after ligation. On exposing the vessels by dissection, and on superficial examination, it seemed as if the loops of the ligatures were unaltered.

Fig. 38—Site of Kangaroo tendon ligature which had been applied 77 days previously around the carotid of an ass (x 90).

The tendon has entirely disappeared, but its site is clearly marked by a mass of new tissue. The outer boundary of the mass where absorption first took place is formed of well-developed fibrous tissue, while the central area consists of young connective tissue.

Fig. 39—Double lateral implantation of the median nerve into the ulnar nerve.—(British Journal of Surgery, Vol. XI.).

The black lines on the forearm show approximately the operation performed. The intrinsic muscles of the hand supplied by the median nerve recovered as is shown in the two lower photographs. For all purposes the hand is a useful hand. He does not employ it for writing, because he has become accustomed to use the left hand for this purpose. Thirty-four months after the operation he was examined by the committee on nerve injuries. Sensibility to cotton wool was absent over the terminal phalanges of the index and middle fingers. The man at that time was back at work. The condition of the hand is in no small measure due to the fact that on returning to England he came under the care of Mr Joyce, of the Reading War Hospital. The operation was performed at Malta in September, 1917.

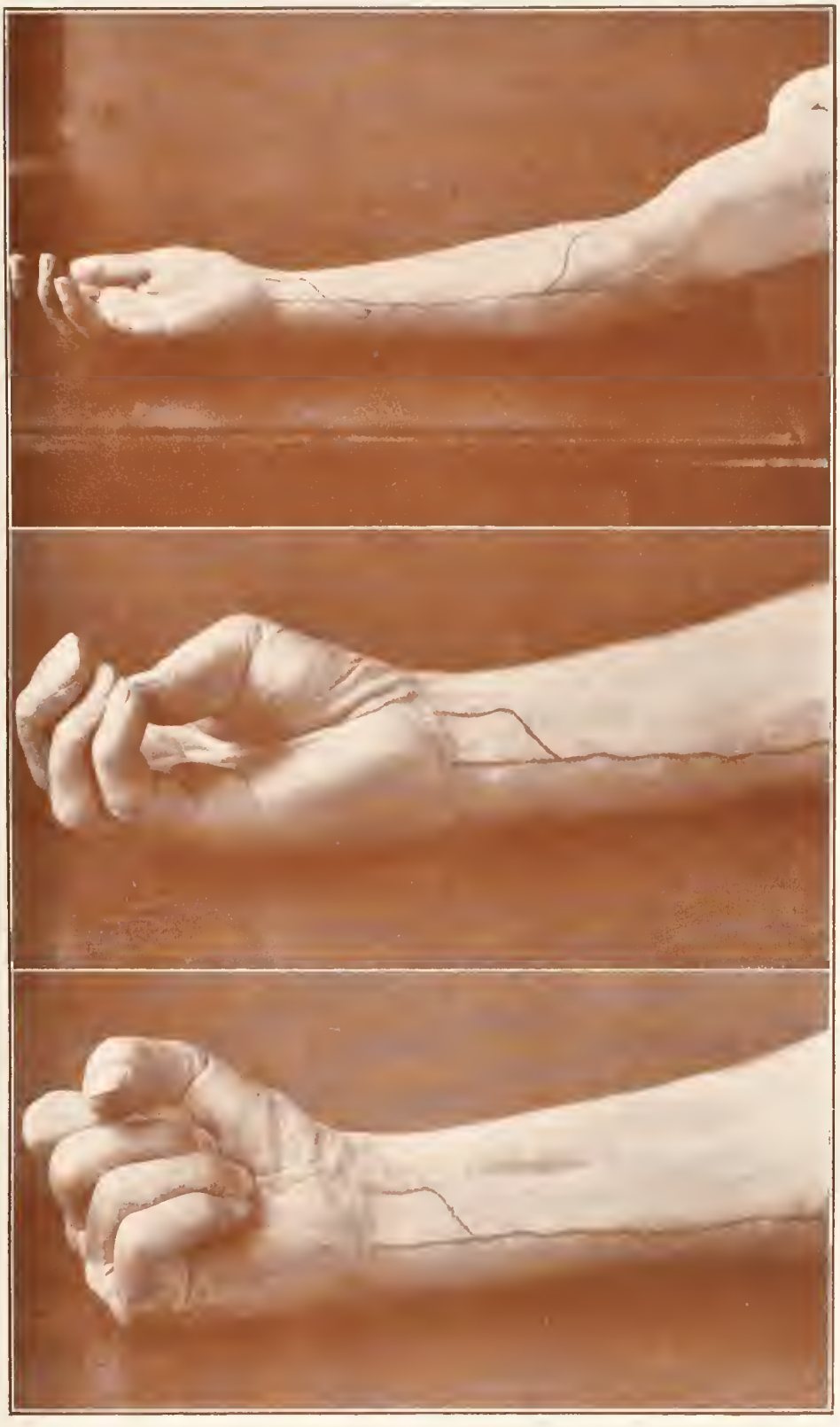


Fig. 39.

Fig. 40 — Monkey — Double lateral implantation of the ends of the divided median nerve of the forearm into the side of the ulnar nerve—Weigert stain for the medullary sheath. The specimen was obtained $10\frac{1}{2}$ months after the performance of the experiment.

The figure shows both the central and distal anastomoses. It would appear that the fibres of the distal segment of the median nerve have formed connections (a) with the fibres in the new tissue on the median side of the ulnar nerve trunk, and (b) with a band of fibres of the main ulnar nerve trunk. These connections are also obvious in the Strœbe stained drawing.

The intrinsic muscles of this hand supplied by the median nerve recovered normal electrical reactions.

Fig. 41—Monkey—Double lateral implantation of the ends of the divided median nerve of the forearm into the side of the ulnar nerve.—Strœbe stain for the axis cylinder—x 20. The specimen was obtained $10\frac{1}{2}$ months after the performance of the experiment.

1.—Parts of the ulnar nerve central to the distal anastomosis.

2.—The distal anastomosis. A portion of the uninjured ulnar nerve takes a share in the anastomosis.

3.—The axis cylinders of the regenerated median nerve beyond the distal anastomosis. On stimulating separately the median and ulnar nerves central to the proximal anastomosis, contraction of the intrinsic muscles of the hand supplied by the median nerve occurred.

4.—The undamaged part of the ulnar nerve beyond the distal anastomosis.

The intrinsic muscles of this hand supplied by the median nerve regained normal electrical reactions.

PART OF THE ULNAR N. ISOLATED BY INCISIONS INTO WHICH THE DIVIDED ENDS OF THE MEDIAN N. WERE SUTURED. THIS PART HAS REGENERATED AND THROUGH IT IMPULSES PASS FROM THE PROXIMAL TO THE DISTAL PORTIONS OF THE MEDIAN N.

ULNAR NERVE FIBRES EXTERNAL TO PORTION OF ULNAR NERVE BETWEEN THE 2 ANASTOMOSIS.

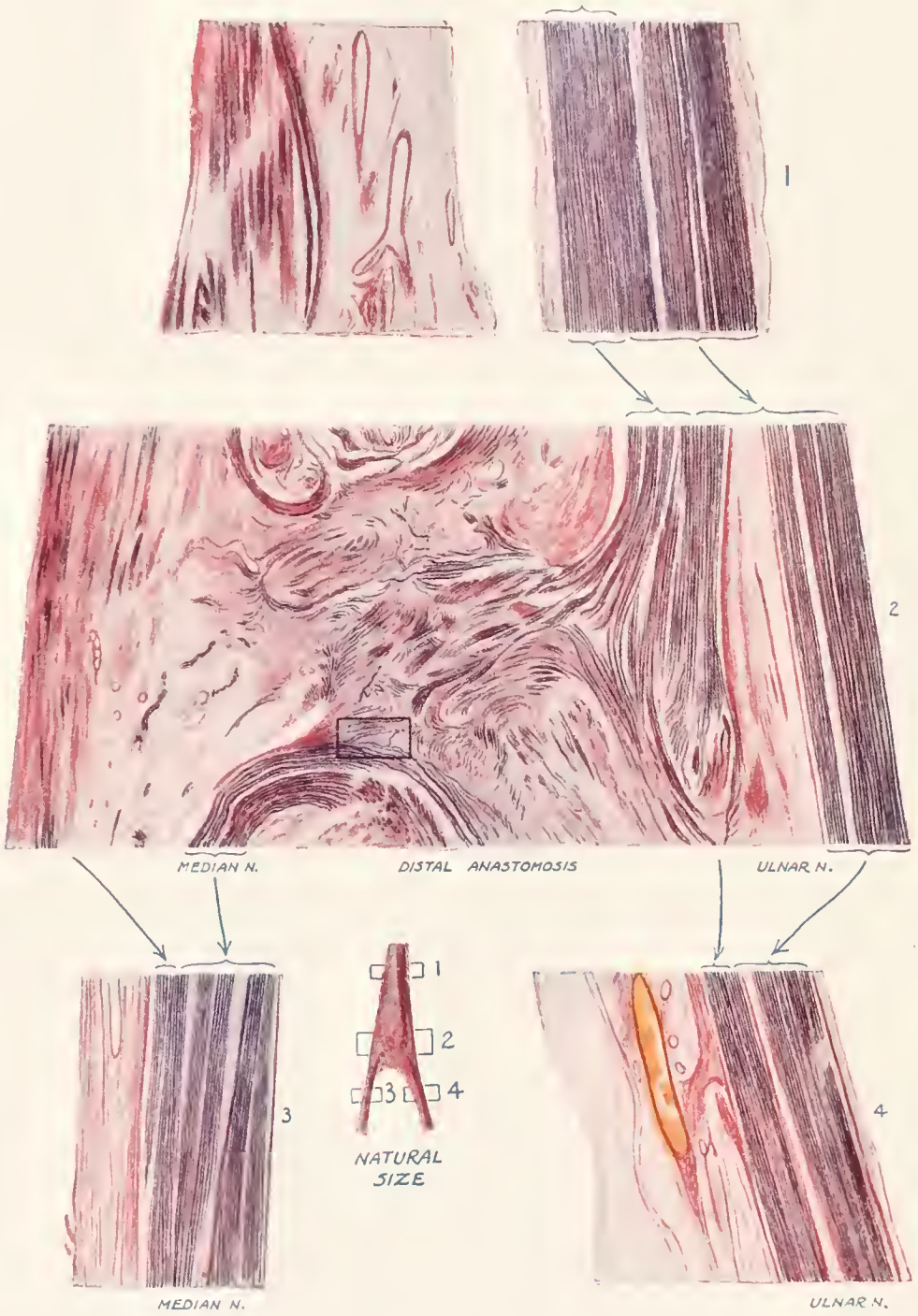


Fig. 41.

Fig. 42—A piece of mammary scirrhus incubated on Agar at 100° F for five days and then left at the room temperature for five months.

The tube was sealed with a rubber cap. No growth of micro-organisms occurred. The piece of carcinoma remained without visible change.

Fig. 43—Section of a portion of scirrhus carcinoma of the breast incubated on solidified blood serum (of the sheep) for 8 days at 100° F. The tube was sealed with a guttapercha cap. No growth of micro-organisms occurred. Note, the migration of chromatiniferous granules from the nuclei.

Fig. 44—Section of the healthy kidney of the dog incubated on solidified blood serum for 8 days at 100° F.

Note, there is no migration of chromatiniferous granules from the nuclei of the epithelial cells.

Fig. 42.

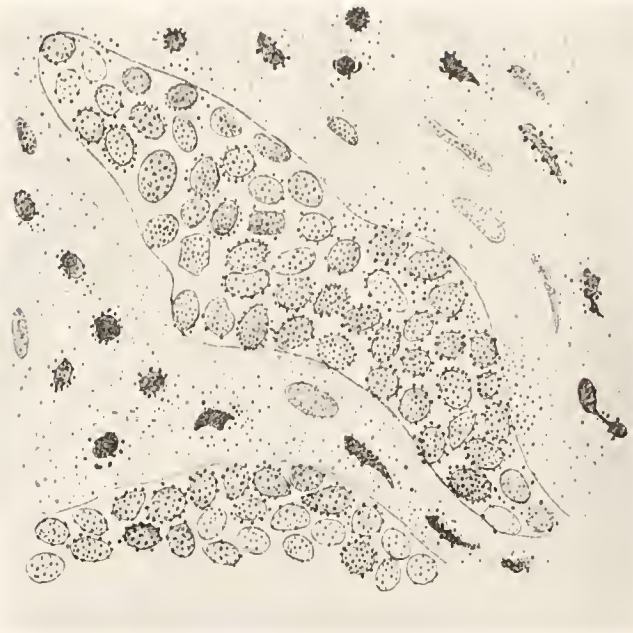


Fig. 43.

Fig. 44.

NOTE I.

Pre-Listerian Surgery.

Those who have recently joined the profession cannot in any way realise the paralysis of surgery sixty years ago in the presence of suppuration, cellulitis, erysipelas, septicæmia, pyæmia, acute traumatic gangrene, and tetanus, for which diseases there was as yet no means of prevention and no remedy.

When I entered St Thomas' Hospital in 1875 nearly all operation cases, and they were very few in number suffered from one or more of the wound diseases already mentioned. I remember an operation for hæmorrhoids in which the patient died a week later from secondary hæmorrhage, pyæmia, and tetanus. [1] All septic cases were removed to No. 8 Block of St Thomas' Hospital and were treated as a rule by numerous incisions, by chlorinated-soda poultices and internally by perchloride of iron and unlimited brandy. Not a few of these patients, after prolonged periods of illness, recovered. The operating theatre was of wood. The auditorium would seat several hundred persons. Each of the four surgeons had some two hours allotted to him for the performance of the ordinary operations of the week. The surgeon operated in a frock coat which had for a long time been kept in the theatre. It was stained with the blood and pus of previous operations. The instruments were placed in a tray lined with green baize. When a ligature was required the theatre attendant

1. (i) A case of tetanus, following ovariotomy, by Knowsley Thornton. Royal Med.: Chir.: Trans.: 1887.
(ii) On tetanus as a complication of ovariotomy, by John Philips. R. Med.: Chir.: Trans.: 1892.
John Philips' case occurred in 1888. Sixty-three other cases are given in a table. He suggested nerve irritation as a cause of tetanus, though he refers to Kitasato's paper, "Uber den Tetanus Bacillus," Zeitschrift fur Hygiene, 1889.

would put it on the stretch between his teeth and the fingers of the left hand. It was then waxed and handed to the surgeon.

St Thomas' Hospital is greatly indebted to Sir William MacCormac [2] for his advocacy and practice of the methods of Lister. As a house surgeon in 1880 I was given an amputation to perform. I used the method of antisepsis I had learned from Lister. I employed Neuber's [3] decalcified bone drainage tubes which had recently been sent to me from Germany. The dressing was removed on the 14th day. The wound had healed without pain or fever. I was advised on several occasions, as was the common practice then, to remove the dressing and inspect the wound. This I refused to do. Neuber's drainage tubes could not be removed. They were firmly held within the stump by the living cells, whose function it was to absorb and replace them. Hence the protruding ends of the tubes were cut off with scissors flush with the surface.

Volkmann in 1871, in consequence of the deaths from pyæmia being so numerous in his hospital, made up his mind to close it altogether for a time. Similar facts were published by Nussbaum, of Munich. Pyæmia was rife in the hospital, and during 1873 hospital gangrene attacked 50 per cent. of all wounds. Before the employment of antiseptic methods, Lister's death rate for amputation was 45 per cent. [4] The legend over the doors of the Hôtel Dieu in Paris is, "This is the House of God and the Gate of Heaven," but when a fire occurred the cry went up, "Let the Hospital burn, and save the sick." In the

2. Antiseptic Surgery by Sir William MacCormac, 1880, p. 149.

3. Dr Neuber, of Kiel: Langenbeck's Archiv., Vol. XXIV., 1879, and Vol. XXV., 1880.

4. Lister's collected papers, Vol. I., p. xix.

beautiful story of "Rab and His Friends" [5] is told how the Reaper, whose name is Death, destroyed even in the wards of the most famous of Edinburgh surgeons.

The pageant of surgery through which I have lived has been the most glorious of all time. A French surgeon [6] thus describes the revolutionary change:—

> "By what miracle has the slender seedling full of sap become the vigorous tree beneath the shade of which works our restless activity, ever in search of new triumphs? You know it too well for me to tell it again after so many others. But far less can you know the impressions produced on the mind of a surgeon who, entering on his career at the epoch of **limited surgery**—the surgery of erysipelas and purulent infection—has marched on with quite an army of followers of the new doctrine to the conquest of the immense progress promised by its gifted initiators, and largely realised by the logical sequence of facts. But I am one of the men of that privileged generation, and the witness of a wonderful revolution. I have known that **deceptive surgery,** with more grave disasters than successes, **that surgery** from which safety was banished even in its smallest undertakings, **that surgery** which had always at its side the danger of death, and poisoned with heavy cares the mind of the operator, **that surgery**. in fine, which saw itself reduced to laying down the knife, as mortal complications fell with impartial fatality on all the operation cases in a ward."

It was Louis Pasteur and Joseph Lister who blazed the pathway for the rise of modern surgery. The issues

5. "Rab and His Friends," by Dr John Brown. 1897.

6. Le Dentu, Clinique Chirurgicale. 1904. Lecon d'Ouverture, p. xi.

were great! the men were great. Their struggles were great, they battled with custom, prejudice and disease. The moral enthusiasms of Pasteur and Lister infused into their themes of action the epic spirit of incomparable ardour. "Post nubila Phœbus." Lister, after years of labour, vanquished pain, disease, and death.

NOTE II.

Some Personal Memories of the Years 1880-1890.

To indicate how recent is our knowledge of bacteriology, I may mention that I attended a lecture in 1880 by Sir John Burdon Sanderson. The subject was the nature of scrofula. He described how he had gathered dust from St Paul's Cathedral, from Westminster Abbey, and from his own drawing-room, and how it had been placed under the skin of a series of guinea pigs. The result, we were told, was that all the guinea pigs were infected with scrofula, and that the disease could not be a specific one, as the specific agent could not be supposed to be in all these three places at the same time. The following year (1881) Koch demonstrated the bacillus of Tubercle.

At the meeting of the physiological section of the International Medical Congress in 1881 David Ferrier demonstrated the truth of the great doctrine of cerebral localisation. I was present at this demonstration. Its transcendent importance was recognised. Ferrier delivered the Marshall Hall oration in 1883. He said:

> "that up to that time cerebral localisation had been absorbed like latent heat by medical science itself as distinct from medical and surgical practice; but that the unfailing safety of experiments upon animals made it clear that similar results would soon be achieved on man himself." (1)

1. R. Med. Chir. Soc. Trans., 1884.

This forecast of Ferrier soon became true. Rickman Godlee removed in London a brain tumour on November 25th, 1884. [2]

In 1885 I attended the first class in bacteriology ever formed in the ancient University of Leipzig. Becker, Koch's first assistant, in full uniform met us every day for two hours for six weeks. Each member of the class had to prove the specificity of each known pathological organism, by himself carrying out to the satisfaction of the lecturer Koch's four postulates. The cholera spirillum had been isolated by Koch the previous year. A member of the class was attacked by cholera, but recovered. I learnt more by attending this class than I ever did in any other six weeks of my life. When I returned to England I brought with me cultures of all the known pathological organisms. I showed them at a meeting of the Pathological Society. I suggested that soon bacteriology would have to be added to the students' curriculum. I remember well with what hilarity this proposal was received, especially by the learned —then, Dr Norman Moore.

My chief object in going to Leipzig in 1885 was to ligate arteries. The frequent occurrence of secondary hæmorrhage in the surgical wards of St Thomas' Hospital had made a great impression upon me. In one ward at the same time I remember there were five cases of secondary hæmorrhage. Birch-Hirschfeld, the Professor of Pathology in the University of Leipzig, who had succeeded Cohnheim, gave me, a young unknown surgeon, a most hearty welcome. He himself assisted me at each experiment, and I tied many arteries in his laboratory. In Leipzig also I attended the operating theatre of Thiersch. On one

. R Med. Chir. Soc. Trans., 1885.

occasion I saw him (with his two able assistants), excise the pylorus for carcinoma. This was the first operation of this type done in Leipzig. The operation had been practised many times in the dead-house, and the six hands worked as a unit. The operation lasted 55 minutes. Three weeks later the patient in the ward was seen eating a chop. In Leipzig, too, I got to know His and Ludwig slightly, and on returning to England brought back the models of the organs by His for the anatomical department of St Thomas' Hospital. The bacteriological class being held in the afternoon, I often took the 6 a.m. train to Halle to attend Volkmann's operations. The first question he asked me was, "Do you know Lister?" and this was the question always asked me whenever I entered at that time a German surgical clinic. In the Halle operating theatre there were three tables where operations were carried out by Volkmann's three assistants. Volkmann himself, taking my arm, walked up and down, making suggestions to the operators and smoking a long cigar. As Volkmann at that time was studying resection of the rectum for carcinoma, he was only doing rectal excisions. These excisions were carried out from the perineum. No vessel was tied till the portion of gut was removed—this took about eight minutes. The view was not obscured by blood, because a garden hose was led down from a huge tank fixed against the ceiling of the large operating theatre. The tank contained 1 in 1000 perchloride of mercury solution and the garden hose conveyed large quantities of the solution to the wound. I remember one morning a simple ovarian cyst was removed, and then the abdomen was irrigated with gallons of 1 in 1000 perchloride of mercury solution. The woman recovered after an anxious illness; vomiting and bloody stools being the striking symptoms. The antiseptic

treatment of wounds was a necessary stage in the evolution of cleanliness.

Before returning to England I went to Berlin, and visited Professor von Bergmann's clinic. I met there the Professor's first assistant, Fehleisen, whose nickname was "Erysipelas coccus," because he was injecting cases of carcinoma mammæ with pure cultures of the erysipelas organism. No doubt this was the origin of the toxin treatment of sarcoma advocated by my friend, William B. Coley. In Berlin, too, I attended lectures by two famous men, Virchow and Helmholz.

When I returned to England in the late summer of 1885 I experienced great good fortune in my personal environment. In 1882 I had lived in the same house with Walter Edmunds and Charles Sherrington, and they were still at work in the Hospital and School. Samuel Shattock was in the Museum of the Medical School, and Victor Horsley was not far off at the Brown Institution. A little later I came to know Marcus Beck, a fine surgeon and a very remarkable man. He took much interest in the absorption of ligatures and in the formation of scar tissue, two subjects which were engaging my attention.

Harvey Cushing was in London in 1892. I remember him as a quiet, reserved, earnest, thoughtful young surgeon. Ten years later I visited the John Hopkins Hospital at Baltimore. He had founded and developed, with the co-operation of the mighty Halsted, the finest surgical neurological department in the world. From this date the friendship of Harvey Cushing has been one of the happiest adventures of my life.

"John Hunter was the greatest man in the combined characters of physiologist and surgeon that the whole annals

of Medicine can furnish." * He awoke in the minds of his pupils a desire to explore the old ground by the new experimental method, and to unearth truths long concealed. Harvey Cushing, scholar, physiologist, experimentalist and surgeon has also lighted a torch. His pupils are carrying it forward in the race. They will pass it on, not only undiminished, but burning with a brighter flame.

The research on the ligation of arteries [3] was continued with my friend, Walter Edmunds. We also did some experiments on intestinal and gastro-intestinal anastomosis. [4] At this time plates, buttons, bobbins, and rubber air bags were fashionable. We came to two conclusions, (a) that suturing of the intestine requires but a needle and thread, and (b) that a portion of intestine reversed will not function. Two or three years later I met von Mikulicz, of Breslau: he said, in answer to my question, any surgeon who required ought else but a needle and thread should not be allowed to suture the intestine.

I learnt a great deal from an investigation carried out with Charles Sherrington on the early stages of the formation of scar tissue; [5] and with Walter Hadden I stimulated the motor cortex and internal capsule of the brain of the monkey. [6] Lastly, Samuel Shattock and I settled down to several years' work on the intimate

3. (a) "The ligation of the larger arteries in their continuity, an experimental enquiry." Royal Medical Chirurgical Society's Transactions, 1886.
   (b) Ligation in Continuity — MacMillan, 1891.
4. (a) "Observations and Experiments on Intestinal and Gastro-Intestinal Anastomosis." Royal Med. Chir. Soc. Trans., 1896.
   (b) For directions for preparing "decalcified bone plates," see "Intestinal Surgery," Keener—Chicago, 1889, by Nicholas Senn, p. 179.
   The first successful resection of the small intestine at St Thomas' was performed by Sir G. Makins. St Thomas' Hospital Reports, 1884.
5. Formation of Scar Tissue. Journal of Physiology, 1889.
6. Experimental Observations on the Brain of the Monkey, St Thomas' Hospital Reports, Vol. XIX., 1889.

*Sir William Lawrence's Hunterian Oration, 1846.

pathology of carcinoma. [7] My family had been decimated by malignant diseases, and as a student I vowed myself to this investigation. We met in Shattock's room in St Thomas' Hospital Medical School three times a week from seven to eleven in the evening and enjoyed ourselves greatly. At first I was the bacteriologist and he was the microscopist. In these investigations we enjoyed the great interest and support of Sir James Paget. Dr Michael Foster spent one long evening with us. The occasion was the examination of many Petri dishes in which we had, after nine months' culture, found an amœba. Dr Foster watched the movements of an amœba on the warm stage while I fished for fresh specimens between the shallow and the deep in the Petri dishes. Dr Foster's advice to us was, infect many fresh Petri dishes: in other words, to repeat the experiment. We did so, but after twelve months the amœba did not reappear ! I may mention also that Sir James Paget gave me great encouragement in the research on the ligation of arteries. He placed at my disposal all his private notes relating to cases of aneurysm and the ligation of arteries.

Within a few years of commencing these various investigations, to my surprise I had correspondence and received

7. (a) Cultivation experiments with new growths and normal tissues, together with remarks on the parasitic theory of cancer. Trans: Path. Soc.: 1887.

(b) A note on the histology of sterile incubated cancerous and normal tissues. Trans.: Path.: Soc.: 1888.

(c) An experimental investigation into the pathology of cancer. Proc. Royal Society, 1890.

(d) Abstract of an address by Sir John Simon on some points of Science and Practice, concerning cancer, delivered on Nov. 9th. 1879, with a note of the reasons for considering cancer to be a micro-parasitic disease, by Samuel Shattock and Charles Ballance. St Thomas' Hospital Reports, Vol. XX., 1890.

(e) An attempt to cultivate parasitic protozoa from malignant tumours, vaccinia, molluscum contagium and certain normal tissues together with infective experiments carried out with the culture media, and a note on the treatment of cancer. Proc.: Royal Society, 1895.

(f) General pathology of New Growths—Clifford Allbutt's System of Medicine, Vol. I., 1896; see also

(g) "Some Thoughts on the Nature of Cancer." Surgery Gynæcology and Obstetrics—February, 1929.

visits from some great American surgeons—Nicholas Senn, of Milwaukee; John Murphy, of Chicago; W. W. Keen, of Philadelphia; Halsted, of Baltimore; and Rudolph Matas, of New Orleans.

In 1886 I visited the Pasteur laboratory in Paris [8] and witnessed the kindness and gentleness of Louis Pasteur in his relations with patients and animals. I saw some terrible cases of Russians bitten by wolves. A rabbit was thus infected. It was chloroformed, the chloroform being dropped on a cone of blotting paper held over the nose of the animal. A minute trephine was employed to open the skull, and a small quantity of emulsion of the medulla of a rabbit dead of rabies was injected under the dura mater. When I returned to England from Paris a case of acute traumatic tetanus was in St Thomas' Hospital. I made an emulsion of the medulla of the man dead of tetanus and injected a small quantity under the dura mater of a rabbit in the same way that I had seen Pasteur inoculate a rabbit with the rabies poison. The rabbit died of tetanus. The bacillus of tetanus was not isolated till 1889. I unknowingly had used the tetanus toxin.

8. See a paper by Louis Pasteur in the Medical Times, August, 1884—"Infectious Diseases and Vaccination for Rabies."